Contour®

Meter and test strips
designed for glucose self-measurement
and measurements by health care professionals
manufactured by Bayer HealthCare

Report from an evaluation
organised by

SKUP

The evaluation was ordered by Bayer AS, Norway

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

SKUP/2009/75

The organisation of SKUP

Scandinavian evaluation of laboratory equipment for primary health care, *SKUP*, is a co-operative commitment of NOKLUS[1] in Norway, Department of Clinical Biochemistry (KBA), Hillerød Hospital and DAK-E"[2] in Denmark, and EQUALIS[3] in Sweden. SKUP was established in 1997 at the initiative of laboratory medicine professionals in the three countries. SKUP is led by a Scandinavian *steering committee* and the secretariat is located at NOKLUS in Bergen, Norway.

The purpose of SKUP is to improve the quality of near patient testing in Scandinavia by providing objective and supplier-independent information 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] SKUP in Denmark is placed in Hillerød Hospital, which is one of several hospitals comprising Copenhagen University Hospital. SKUP refers to DAK-E (Danish Quality Unit of General Practice), an organisation that refers to KIF, founded by Danish Regions and PLO (The Organisation of General Practitioners in Denmark).

[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
Hillerød Hospital
Klinisk Biokemisk Afdeling
Dyrehavevej 29, indgang 16A
DK-3400 Hillerød
+45 48 29 41 76
esj@hih.regionh.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 Bayer AS.

1. Summary

Background
Contour blood glucose meter and Contour test strips are designed for glucose self-measurements performed by diabetes patients and measurements performed by health care professionals. The meter and the test strips are produced by Bayer Healthcare and supplied in the Nordic countries by Bayer. Contour was launched onto the Scandinavian market in 2006. Bayer turned to SKUP for an evaluation of Contour in order to get an assessment of the analytical quality of Contour according to a quality goal suggested by NOKLUS in 2008 for glucose instruments used in primary care centres and nursing homes. The quality goal allows a total error of 10%. The evaluation of Contour was carried out under the direction of SKUP from March to September 2009.

The aim of the evaluation
The aim of the evaluation of Contour was to

- assess the analytical quality under standardised and optimal conditions, performed by a biomedical laboratory scientist in a hospital environment
- assess the analytical quality by intended users in three primary care centres
- discuss achieved total measurement error according to a quality goal of 10%, suggested by NOKLUS as a quality goal for glucose device used in primary care and nursing homes
- examine the variation between three lots of test strips
- examine if hematocrit interferes with the measurements
- evaluate Contour regarding user-friendliness

Materials and methods
Capillary samples from 88 persons with diabetes and 10 healthy individuals were collected in a hospital laboratory. Two measurements on Contour were carried out for each person, and capillary samples were directly prepared for measurements with a designated comparison method. In addition a sample for hematocrit was taken. In three primary care centres a total of 119 capillary samples were measured in duplicate on Contour. Three different lots of test strips were used. The evaluators answered questionnaires about the user-friendliness of Contour.

Results

- The precision of Contour was good. The repeatability CV was approximately 4%, obtained under standardised and optimal conditions as well as when the measurements were performed in three primary care centres. The suggested quality goal for precision was obtained.
- For glucose concentrations <10 mmol/L Contour gave results in agreement with the comparison method. For glucose concentrations >10 mmolL the results on Contour were systematic lower than the results from the comparison method. The bias at this concentration level was -0,47 mmol/L (- 3,6%).
- The accuracy of Contour was good. The results fulfilled the quality goal proposed in ISO 15197. The total error of Contour was approximately 10%, coinciding with the suggested quality goal for use in Norwegian primary care centres and nursing homes.

- Two of the three lots of Contour test strips gave glucose results in agreement with the comparison method. The third lot gave lower results than the comparison method, with a systematic deviation of approximately -0,3 mmol/L.
- The glucose measurements on Contour did not seem to be affected by hematocrit values from 27 – 49%.
- The evaluators thought that the Contour device was user-friendly and easy to operate.

Conclusion

The precision of Contour was good, with a repeatability CV of approximately 4%. The accuracy of Contour was good. The calculated total error was approximately 10%. Suggested quality goals were obtained. Glucose measurements on Contour did not seem to be affected by hematocrit in this study. The users found the Contour device easy to use.

Comments from Bayer AS

A letter with comments from Bayer AS is attached to the report. Please see attachment 10.

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. Contour is designed for monitoring blood glucose, and it is reasonable to set the quality goal 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
The quality goal set by ISO 15197, *In vitro diagnostic test systems – Requirements for blood glucose monitoring systems for self-testing in managing diabetes mellitus* [4] applies for glucose self-measurements, and has been used as quality goal for previous user evaluation among diabetes patients organised by SKUP [5,6]. The ISO-guide is an international protocol for evaluating meters designed for glucose monitoring, and 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.

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. In 2008 NOKLUS suggested quality goals for glucose instruments for use in primary care centres and nursing homes in Norway [7]. This quality goal is in accordance with the quality goal set by ADA. When Bayer turned to SKUP for an evaluation of Contour, the intention was to get an assessment of the analytical quality of Contour according to the quality goal suggested by NOKLUS.

The Contour results in this evaluation will be discussed according to the following analytical quality goals:

Precision, CV<5%
Total error <10%

3. Materials and methods

3.1. The Contour device

Contour is a blood glucose monitoring system based on biosensor technology. The system consists of a Contour meter and dry reagent test strips, Contour test strips. The system is designed for capillary blood glucose testing performed by persons with diabetes or by health care professionals.
The system requires a blood volume of 0,6 µL. The measuring range is 0,6 – 33,3 mmol/L. The result is shown within 5 seconds. Contour reports plasma glucose values. The system requires no calibration. The memory can store 480 results.

Test principle of Contour
The enzyme GDH+FAD oxidizes glucose to gluconolactone. Electrons from the glucose are transferred to the oxidized form of the mediator ferricyanid, thereby converting the mediator to the reduced form. The mediator in turn delivers the electrons to the electrode. This step is measured as an electrical current by the meter. The current is directly proportional to the concentration of glucose into the sample.

$$Glucose + Mediator_{ox} \xrightarrow{FAD+GDH} Gluconolactone + Mediator_{red}$$

$$Mediator_{red} + electrical\ potecial \rightarrow Mediator_{ox} + e^-$$

3.1.1. Product information, Contour

The Contour blood glucose meter system is manufactured by Bayer HealthCare.
Technical data from the manufacturer is shown in table 1.
For more details, see attachment 1; Facts about the Contour system (in Norwegian).

Table 1. Technical data from the manufacturer

TECHNICAL DATA FOR CONTOUR	
Optimal operating temperature	5 – 45 °C
Sample volume	0,6 µL
Measuring time	5 seconds
Measuring range	0,6 – 33,3 mmol/L
Hematocrit	0-70%
Memory	480 test results
Power source	Two 3-volt lithium batteries (DL2032 or CR2032)
Operating time	Approximately 1000 tests
Humidity	10 – 93 % RH
Dimensions	77 mm x 57mm x 19 mm
Weight	47,5 g

Contour serial no
Contour with serial number 2074174 was used under standardised and optimal conditions by the biomedical laboratory scientist.
Contour with serial numbers 2074142, 2074155 and 2074225 were used at three primary health care centres.

Contour test strips:

Lot A, lot no 9BC3D01	Expiry 2011-02
Lot B, lot no 9BC3D06	Expiry 2011-02
Lot C, lot no 9BC3C06	Expiry 2011-02

Contour Control solution:
The Contour Control is an aqueous solution with D-glucose in 99% non-reactive ingredients.
Control Normal, lot no 1741098 Expiry 2010-09 Target value 6,0 – 8,3 mmol/L

Suppliers of Contour in the Nordic countries:

Denmark:
Bayer A/S
Diabetes Care
Postboks 2090
DK-2800 Kgs. Lyngby

Phone: +45 45 23 50 00
www.bayerdiabetes.dk

Norway:
Bayer AS
Diabetes Care
Postboks 14
N-0212 Oslo

Phone: +47 24 11 18 00
www.bayerdiabetes.no

Sweden:
Bayer AB
Diabetes Care
Box 606
S-16929 Solna

Phone: +46 (0)8 580 22300
www.bayerdiabetes.se

Finland:
Bayer Oy
Diabetes Care
PL 13
FIN-02271 Espoo

Phone: +358 9 887 887
www.bayerdiabetes.fi

3.2. 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 [8] 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 [9]. The controls are included in NOKLUS's External Quality Assessment program. The results are summarized in chapter 5.1.3.

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 the measuring series in this evaluation. The results are shown in attachment 2.

3.2.1. Product information, the comparison method

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

Glucose reagent
Lot 72041HW00 Expiry 2009-09

Calibrator
Multiconstituent Calibrator
Lot 63421M100 Expiry 2009-09-30 Reference value, cal 1 = 5,27 mmol/L
Reference value, cal 2 = 24,42 mmol/L

Internal quality controls
Autonorm Human Liquid 1 and 2, SERO AS
Liquid 1: Value = 3,50 ±0,21 mmol/L Lot 0802102 Expiry 30.04.10
Liquid 2: Value = 14,92 ±0,75 mmol/L Lot 0806267 Expiry 31.08.10

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 2009-12-31
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 7074501 Expiry 2010-10

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

3.3. Planning of the evaluation

Background for the evaluation
Contour is a blood glucose monitoring system designed for capillary blood testing performed by diabetes patients or by health care professionals. The Contour-system is produced by Bayer Healthcare and supplied in Scandinavia by Bayer. The system was launched onto the Scandinavian market in 2006. Bayer turned to SKUP for an evaluation of Contour to get an assessment of the analytical quality of Contour according to a quality goal suggested by NOKLUS in 2008. This quality goal allows a total error up to 10%, and was suggested for glucose instruments used in primary care centres and nursing homes [7].

Inquiry about an evaluation
Torstein Myhre, Bayer HealthCare, applied to SKUP in November 2008 for an evaluation of Contour glucose meter with Contour test strips, with focus on assessment of analytical quality when used in primary health care. SKUP accepted to carry out this evaluation on behalf of Bayer.

Protocol, agreements and contract
The arrangement for an evaluation was agreed upon in January 2009 and the evaluation contract was signed in February. SKUP made a proposal for an evaluation protocol in February 2009. The protocol was approved in March.

Evaluation sites and persons involved
The evaluation took place in Moss Hospital, Norway, and in three primary care centres in Bergen. Biomedical laboratory scientist, Torny Bjerketvedt, Moss Hospital, was appointed on contract for the practical work concerning the evaluation under standardised and optimal conditions. Primary care centres in Bergen were contacted by advisory biomedical laboratory scientist Hilde-Kristin Rondestveit, NOKLUS. Allmennmedisin Aasegården, Laksevåg legesenter and Legehuset Varden agreed to take part in the evaluation. The staff at the three primary health care centres were guided and supported along the way by Hilde-Kristin Rondestveit.
Allmennmedisin Aasegården is a small primary care centre with one physician and one health secretary. Health secretary Hildegunn Normann Iversen assumed the responsibility with the practical work with the evaluation.
Three physicians, two medical secretaries and one health secretary work at Laksevåg legesenter. The three secretaries Kjellaug Folkedal, Berit Hagen and Marianne Jansen were assigned to carry out the evaluation project together.
The largest of the tree centres is Legehuset Varden, with six physicians and a post for an intern doctor, and four medical- and health secretaries as co-workers. Medical secretary Anita Kokai and health secretary Ellen Marie Grøsvik Skogvold took on the responsibility with the practical work with the evaluation.
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. Biomedical laboratory scientist Grethe Kalleklev was given the responsibility for the practical work in the laboratory. The statistical calculations and the report writing are done by Grete Monsen and Camilla Eide Jacobsen, SKUP/NOKLUS in Bergen.

Preparations and training program
The preparations for the evaluation started in January 2009. The meters and test strips for the evaluation were received in March. In the beginning of April Torny Bjerketvedt was trained for the practical work with Contour by Victoria Helander, Bayer. Ann Kristin Rasmussen, Bayer, trained the personnel in the three primary care centres. The training session corresponds to ordinary training for new users.

Sampling
Capillary samples from 88 persons with diabetes were collected in the hospital laboratory in Moss Hospital. The persons with diabetes were not hospitalised, but were recruited over time among outpatients, for a number of various glucose evaluation studies. The recruitment was effected through advertisements in three local newspapers, by mail inquiry sent to the members of the local branch of The Norwegian Diabetes Association, and through an advertisement in "Diabetes", a magazine for the members of The Norwegian Diabetes Association. In addition ten colleagues at NOKLUS volunteered their services as candidates for sampling of healthy individuals.
Two measurements on Contour were carried out for all 98 participants. For the 88 diabetes patients, two capillary samples were directly prepared for measurements with a designated comparison method. Similarly, one capillary sample from each of the healthy individuals was prepared. I addition a sample for hematocrit was taken of the diabetes patients.
In three primary care centres a total of 119 capillary samples were measured in duplicate on Contour. There was no sampling for the comparison method in primary health care.

3.4. The evaluation procedure

3.4.1. The model for the evaluation of Contour

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*" [10].
The evaluation of Contour comprises the following:

- assess the analytical quality under standardised and optimal conditions, performed by a biomedical laboratory scientist in a hospital environment
- assess the analytical quality by intended users in three primary care centres
- discuss achieved total measurement error according to a quality goal of 10%, suggested by NOKLUS as a quality goal for glucose device used in primary care and nursing homes
- examine the variation between three lots of test strips
- examine if hematocrit interferes with the measurements
- evaluate Contour regarding user-friendliness

Blood sampling
The Contour meter was checked by means of the manufacturer's control solution every day it was used. The samples for Contour, as well as the samples for the comparison method, were collected from finger capillaries. The sampling sequence was started with a sample for the comparison method and followed by two measurements on Contour, before a second sample for the comparison method was taken. Finally 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 the Contour test strips states that the influence of hematocrit on the glucose measurements is not of significance for hematocrit values from 0 to 70%.

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 (300 µL) 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 [8].

The samples were analysed on an Architect instrument in the end of August and the beginning of September 2009. The samples were thawed at NOKLUS just before they were analysed.

Stability of the glucose concentration during the sampling time
For each sampling sequence, two samples for the comparison method were collected. These pairs of samples, taken before and after the measurements on Contour, 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 first and second result is looked upon as the estimate of the true value of the sample. To secure the decision regarding the stability of the glucose concentration, all the second samples were analysed in duplicate.

Assessment of the glucose concentration stability
According to ISO 15197, the difference between the first and the second comparative reading must not be more than 4% or 0,22 mmol/L. This is a strict demand. Several samples in the evaluation had a difference just over 4%. After a general evaluation of all the results, the paired measurements with differences between 4 and 10% were included in the calculations, as they did not affect the outcome of the assessment of accuracy or bias. The conclusions in the report are not dependent on keeping or excluding these results.
Deviations >10% are regarded as not acceptable. Such results are always excluded, and the matching meter results removed before assessment of accuracy and hematocrit influence, and before calculation of trueness and total error. This applied to ID 14 and ID 45.

Evaluation of the user-friendliness
The user-friendliness of Contour was evaluated by means of questionnaires drafted by SKUP. The evaluators filled in questionnaires about the information in the manual or package insert, about time factors, quality control possibilities and about the operation facilities. The questionnaires and the users' assessments are presented in chapter 5.4.

4. Statistical expressions and calculations

4.1. Statistical terms and expressions

The definitions in this section come from ISO/IEC Guide 99; International Vocabulary of Metrology, VIM [11].

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

Capillary samples from 88 persons with diabetes and 10 healthy individuals were collected in a hospital laboratory. In three primary care centres a total of 119 capillary samples were measured in duplicate.

4.2.2. Statistical outliers

The criterion promoted by Burnett [12] 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, the following results are missing or excluded for other reasons:

From the evaluation in the hospital laboratory
ID 50: The patient was unable to go through with the evaluation
ID 14 and ID 45: The glucose concentration was not stable enough during the sampling time
ID 86: The first of the two samples for the comparison method is missing. To get an estimate of the true value of the glucose concentration for this patient, the mean of the duplicate measurement of the second sample is used alone.

From the evaluation in primary health care
ID 40: Primary health care centre C, only one result, and is therefore not included in the calculation of imprecision.

4.2.4. Calculations of imprecision based on duplicate results

Two capillary samples were taken of each diabetes patient for Contour and for the comparison method. The imprecision was calculated by use of paired measurements [13, 14], 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. The results on Contour achieved under optimal measuring conditions in the hospital laboratory together with the results achieved at three primary health care centres, were combined and checked together. Table 2 shows that no systematic difference was pointed out between the paired measurements. This conclusion is also supported by observations in previous glucose evaluations carried out by SKUP.

Table 2. Comparison of the 1st and 2nd measurements on Contour.

Contour Glucose level (mmol/L)	n	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)
< 7	84*	5,9	5,9	-0,02	-0,10 – (+0,06)
7 – 10	80	8,3	8,3	-0,05	-0,16 – (+0,06)
≥ 10	52	13,0	13,0	+0,08	-0,15 – (+0,32)

*One outlier according to Burnett's model; ID40 in primary health care centre B

4.2.5. Calculation of trueness

To assess the trueness of the results on Contour, 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 Contour. The mean difference is shown with a 95% confidence interval.

4.2.6. Assessment of accuracy

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

4.2.7. Calculation of total error

The total error is the combination of the analytical bias and imprecision according to the linear model:

$$\text{Total error} = |\text{bias}| + z \cdot \sigma$$

where z is the deviate according to a certain probability and σ is the imprecision. The z-value is 1,96 for a two-tailed probability of 0,05, and 1,65 for a corresponding one-tailed probability. Westgard et al [15] use 1,96 for a situation of no bias and 1,65 for the bias situation.

In 2008 NOKLUS suggested a quality goal for glucose instruments for use in primary care centres and nursing homes in Norway, with a total error <10%. At the same time, NOKLUS published a list of glucose meters in the Norwegian marked fulfilling this quality goal. The total error of the various glucose meters was estimated from the imprecision and bias of each device. When Bayer turned to SKUP for an evaluation of Contour, the intention was to get an assessment of the analytical quality of Contour according to this quality goal. The total error of Contour will be calculated in a corresponding way.

5. Results and discussion

5.1. Analytical quality of the designated comparison method

5.1.1. Internal quality control

In daily operation of the comparison method, the analytical quality of the method is monitored with internal quality control solutions at two levels of glucose concentrations. The control results from the evaluation period were inside the limits of the target values for the controls.
The internal quality control raw data is shown in attachment 2.

5.1.2. The precision of the comparison method

Repeatability

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, two capillary samples were taken of each individual for measurement on the comparison method. The blood sampling was carried out with a small time gap between the first and the second sample for each diabetes patient. The paired measurements reflect the stability of the glucose concentration during the sampling time, and not the precision of the method. To achieve a measure for the repeatability of the comparison method, the second sample was analysed in duplicate.
The repeatability of the comparison method is shown in table 3.
The raw data is shown in attachment 3.

Table 3. Repeatability, the comparison method. Results achieved with capillary blood samples

Glucose level (mmol/L)	n*	Outliers	The comparison method mean (mmol/L)	CV% (95% confidence interval)
<7	26	0	6,0	1,4 (1,2 – 2,0)
7 – 10	31	0	8,5	1,2 (0,9 – 1,5)
≥10	40	1**	13,1	1,3 (1,0 – 1,5)

*The given numbers of results (n) are counted before exclusion of outliers. Mean and CV are calculated after exclusion of outliers.
**One outlier (ID27) according to Burnett's model.

Discussion

The repeatability CV was approximately 1,3%. The precision of the comparison method was good.

5.1.3. 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 4.

Table 4. Standard Reference Material (SRM 965a) measured on the comparison method

SRM 965a	Date	Certified glucose concentration mmol/L (uncertainty)	n	Mean value glucose (mmol/L)	% deviation from target value
Level 1	31.08.09	**1,918**	5	1,90	
	01.09.09	(1,898 — 1,938)	5	1,90	
	Total		**10**	**1,90**	**-0,9**
Level 2	31.08.09	**4,357**	5	4,35	
	01.09.09	(4,309 - 4,405)	5	4,37	
	Total		**10**	**4,36**	**+0,1**
Level 3	31.08.09	**6,777**	5	6,92	
	01.09.09	(6,704 — 6,850)	5	6,91	
	Total		**10**	**6,92**	**+2,1**
Level 4	31.08.09	**16,24**	5	16,88	
	01.09.09	(16,05 — 16,43)	5	17,05	
	Total		**10**	**16,97**	**+4,5**

Table 4 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, and just outside the uncertainty limits. All results from Architect were therefore adjusted according to the certified NIST-targets. The adjustment was carried out by means of inverse calibration [16, 17] by the following regression equation: **y = 0,948x + 0,182.**
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 5.

Table 5. Trueness of the comparison method

Control	Date	Target value glucose (mmol/L)	n	Mean value glucose (mmol/L)	% deviation from target value
TM Gluc L-1	31.08.09	4,78	5	4,78	
	02.09.09		5	4,78	
	Total		**10**	**4,78**	**0**
TM Gluc L-2	31.08.09	11,8	5	11,82	
	02.09.09		5	11,86	
	Total		**10**	**11,84**	**0**

Discussion

The trueness of the comparison method is good.

5.2. Analytical quality of Contour used in a hospital laboratory

5.2.1. Internal quality control

The Contour meter was checked with the manufacturer's control solution every day it was in use. All results were within the control range given on the Contour test strip bottle or carton.
The raw data from the measurements with the internal quality control is shown in attachment 4.

5.2.2. The precision of Contour

Repeatability under standardised and optimal measuring conditions in a hospital laboratory
The repeatability obtained with capillary blood samples is shown in table 6.
The raw data is shown in attachment 5.

Table 6. Repeatability. Results achieved with capillary blood samples measured under standardised and optimal conditions

Glucose conc. level (mmol/L)	n*	Outliers	Contour mean (mmol/L)	CV% (95% confidence interval)
<7	27	0	6,0	4,7 (3,7 – 6,3)
7 – 10	40	0	8,5	3,7 (3,1 – 4,8)
≥10	31	0	13,2	4,8 (3,7 – 6,4)

*The given numbers of results (n) are counted before exclusion of outliers. Mean and CV are calculated after exclusion of outliers.

Reproducibility with Internal Quality Control Solution
The reproducibility is assessed with the Contour 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 Contour during the whole evaluation period. The reproducibility of Contour is shown in table 7.

Table 7. Reproducibility. Results achieved with Contour Control N

Contour Control N	n*	Outliers	Target value (mmol/L)	Mean value glucose (mmol/L)	CV% (95% confidence interval)
Stand and opt. conditions	50	0	6,0 – 8,5	7,6	2,2 (1,8 – 2,7)

*The given numbers of results (n) are counted before exclusion of outliers. Mean and CV are calculated after exclusion of outliers.

Discussion, repeatability and reproducibility
As argued for in chapter 2, the precision of glucose meters designed for monitoring blood glucose should give a CV below 5%. The results in table 6 were achieved under standardised and optimal conditions. No results were segregated as outliers according to Burnett. The repeatability CV was <5%. The precision was good. The recommended quality goal for precision is obtained.
The reproducibility on Contour under standardised and optimal conditions was good when measured with Contour Control N. The CV was approximately 2%.

5.2.3. The trueness of Contour

The trueness of Contour is calculated from the results achieved by the biomedical laboratory scientist in the hospital laboratory. The measurements on Contour are performed with three lots of Contour test strips.
The results are shown in table 8.

Table 8. Mean difference between Contour and the comparison method

	Glucose <7 mmol/L		Glucose 7 – 10 mmol/L		Glucose ≥10 mmol/L	
	The comparison method	Contour	The comparison method	Contour	The comparison method	Contour
Mean glucose (mmol/L)	5,91	5,86	8,52	8,36	13,11	12,64
Mean deviation from the comparison method, mmol/L (95% CI)	-0,06 ((-0,19) — (+0,08))		-0,16 ((-0,32) — (+0,01))		-0,47 ((-0,82) — (-0,12))	
n*	26		35		35	
Outliers	0		0		0	

* The given numbers of results (n) are counted before exclusion of outliers

Discussion
No significant bias was pointed out for glucose results on Contour for glucose concentrations up to10 mmol/L. There was a small, but significant bias between Contour and the comparison method at the highest concentrations level. For glucose levels >10 mmol/L, Contour showed significantly lower values than the comparison method. The bias was -0,47 mmol/L.

5.2.4. The accuracy of Contour

To evaluate the accuracy of the results on Contour, the agreement between Contour and the comparison method is illustrated in a difference-plot. The plot shows the deviation of single measurement results on Contour from the true value, and gives a picture of both random and systematic deviation, reflecting the total measuring error on Contour. The total error is demonstrated for the first measurements of the paired results. Three different lots were used. The narrow limits in the plot represent the quality goal suggested by NOKLUS for glucose instruments for use in primary care centres and nursing homes in Norway. This quality goal is also in accordance with the goal set by ADA (se chapter 2, Analytical quality specifications). The wider limits in the plot represent quality limits set in ISO 15197.
The accuracy of Contour, with three lots of test strips is shown in figure 1.

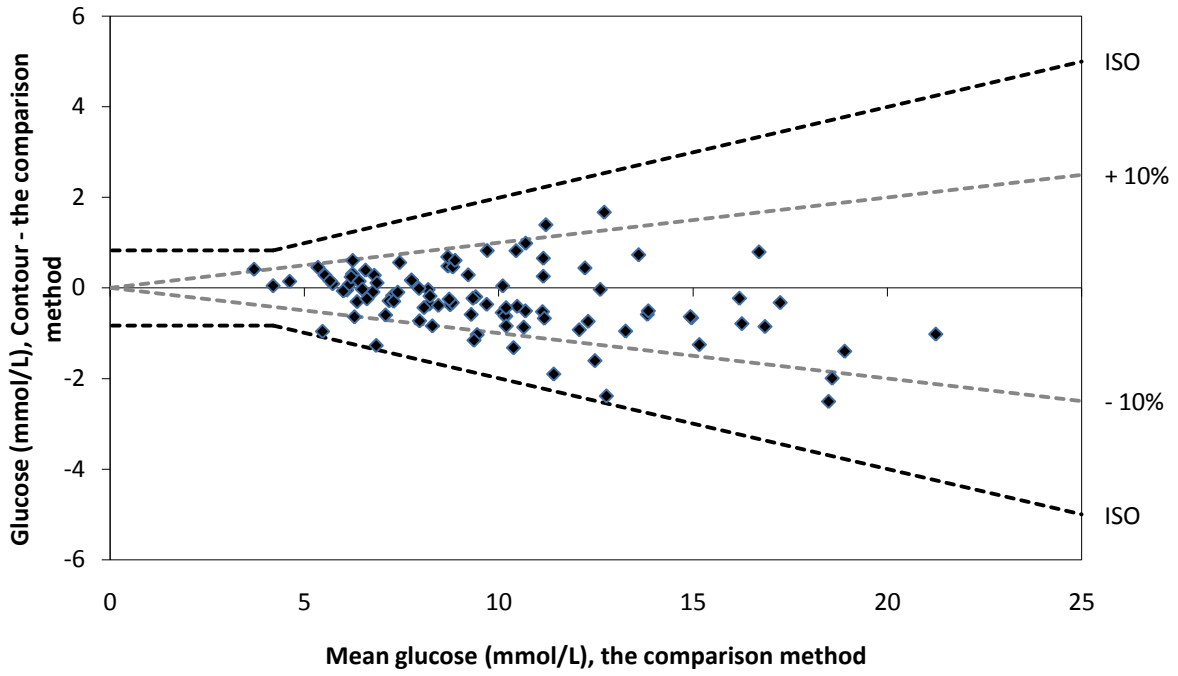

Figure 1. Accuracy. Contour with three lots of test strips under standardised and optimal measuring conditions. The x-axis represents the mean value of the duplicate results on the comparison method. The y-axis shows the difference between the first measurement on Contour and the mean value of the duplicate results on the comparison method. Lines represent quality goal limits set in ISO 15197 and quality goals suggested by NOKLUS for glucose instruments for use in primary care centres and nursing homes in Norway. n = 96

Discussion

The Contour results fulfilled the quality goal proposed in ISO 15197. A calculated Total error is presented section 5.2.5.

5.2.5. Total error

The total error of Contour was calculated as the combination of the achieved analytical bias and imprecision according to the linear model:

Total error = |bias| + z · σ

where z is the deviate according to a certain probability and σ is the imprecision. The z-value is 1,96 for a two-tailed probability of 0,05, and 1,65 for a corresponding one-tailed probability. A z-value of 1,96 is used for the situation of no bias and a z-value of 1,65 for the bias situation. The total error of Contour is shown in table 9.

Table 9. The total error of Contour

Glucose	<7 mmol/L	7 – 10 mmol/L	≥10 mmol/L
CV%	4,7	3,7	4,8
Bias, mmol/L	-0,06	-0,16	-0,47
Bias, %	-1,0	-1,9	-3,6
TE (%) = |bias| + 1,65 · CV	8,8	**8,0**	**11,5**
TE = 1,96 · CV	**9,2**	7,3	
n*	26	35	35
Outliers	0	0	0

* The given numbers of results (n) are counted before exclusion of outliers

Discussion

The total error of Contour was between 8 and 11,5%, depending on the glucose concentration. Assessed as a whole, the total error was approximately 10%, coinciding with the suggested quality goal for use in Norwegian primary care centres and nursing homes.

5.2.6. Variation between three lots of test strips

The measurements on Contour were performed with three different lots of test strips. Each lot was used in a separate group of diabetes patients. Obviously, the mean glucose concentration in the three groups 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 deviation for each of the three lots from the comparison method was calculated (paired t-test), as an indirect measure of the lot variation. The results were sorted according to the lot of test cassettes. To get a sufficient number of results in each group, the deviation of each lot must then be calculated for the whole glucose concentration range together.
The results are shown in table 10.

Table 10. Variation between three lots of test strips.

	The comparison method	Contour Lot 9BC3D01	The comparison method	Contour Lot 9BC3C06	The comparison method	Contour Lot 9BC3D06
Mean glucose (mmol/L)	8,63	8,46	9,36	9,04	10,49	10,34
Mean deviation from the comparison method, mmol/L (95% CI)	-0,17 ((-0,36) — (+0,01))		-0,32 ((-0,55) — (-0,10))		-0,15 ((-0,53) — (+0,22))	
n*	34		37		25	
Outliers	1**		0		0	

* The given numbers of results (n) are counted before exclusion of outliers
** One outlier (ID2) according to Burnett's model

Discussion

There was no provable difference between glucose results achieved with two of the three lots of Contour test strips and glucose results on the comparison method. The two lots gave glucose results in agreement with the comparison method. Glucose results achieved on Contour with lot no. 9BC3C06 were lower than the results on the comparison method. The mean deviation from the comparison method was -0,32 mmol/L. The deviation is small, but statistically significant.

5.2.7. Effect of hematocrit

The product insert of Contour test strips states that glucose measurements are not influenced by hematocrit values from 0 to 70%. To measure the effect of hematocrit on Contour, a hematocrit sample was taken of the diabetes patients (voluntary). The glucose concentration range in the samples was 3,7 – 20,3 mmol/L. The hematocrit range was 27 – 49%.

The effect of hematocrit is shown in figure 2. The x-axis in the plot shows the hematocrit value in percentage and the y-axis shows the difference in glucose concentration between Contour and the comparison method (Contour - the comparison method) in mmol/L. The trend-line is shown in the figure.

The raw data is shown in attachment 6.

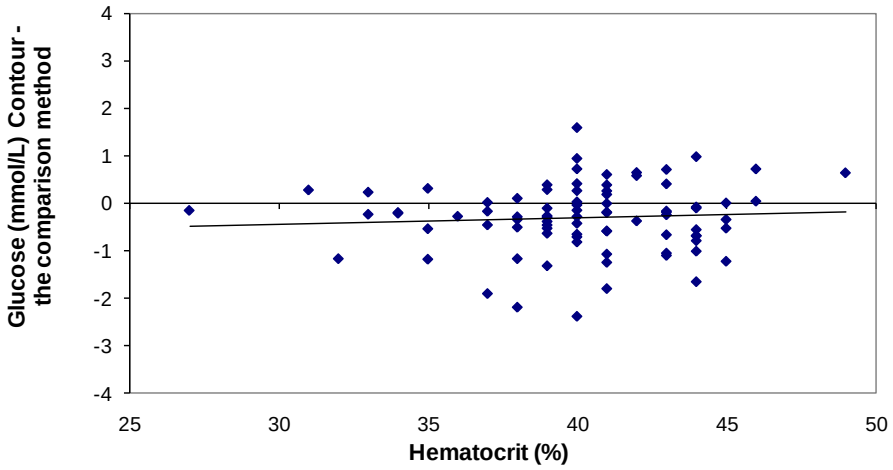

Figure 2. The effect of hematocrit on glucose measurements on Contour. The x-axis shows the hematocrit value in percent. The y-axis shows the difference in glucose concentration between Contour and the comparison method (Contour – the comparison method) in mmol/L. n= 84.

Discussion

Glucose measurements on Contour did not seem to be affected by the hematocrit values of the samples. Samples with hematocrit values outside the range 27 – 49% have not been tested.

5.3. Analytical quality of Contour used in primary health care

5.3.1. Internal quality control

The Contour meter at each of the three primary health care centres was checked with the manufacturer's control solution every day it was in use. All results were within the control range given on the Contour test strip bottle or carton.

5.3.2. The precision of Contour

Repeatability achieved at three primary health care centres

The repeatability obtained at three primary care centres with a total of 119 capillary blood samples is shown in table 11.
The raw data is shown in attachment 7.

Table 11. Repeatability. Results achieved in primary health care

Primary Health Care Centre	Glucose level (mmol/L)	n*	Outliers	Contour, mean (mmol/L)	CV% (95% confidence interval)
A	<7	29	0	5,8	4,1 (3,3 – 5,7)
B	<7	12	1**	6,0	4,1 (3,0 – 7,3)
C	<7	17	0	6,0	4,5 (3,3 – 6,9)
A	≥7	11	0	10,4	3,1 (2,2 – 5,6)
B	≥7	28	0	10,1	5,3 (4,2 – 7,1)
C	≥7	22	0	9,0	4,3 (3,3 – 6,2)

*The given numbers of results (n) are counted before exclusion of outliers. Mean and CV are calculated after exclusion of outliers.
**One outlier (ID40, primary care centre B) according to Burnett's model.

Reproducibility with Internal Quality Control Solution at three primary health care centres

The reproducibility was assessed with the Contour Control Normal at each of the three primary care centres. Artificially produced control materials have other matrix effects than whole blood, and may therefore give other results than results achieved with blood. The reproducibility of Contour in the three primary health care centres is combined and shown in table 12.
The raw data from the measurements with the internal quality control is shown in attachment 3.

Table 12. Contour – Reproducibility (results with Contour Control N)

Contour Control N	n*	Outliers	Target value (mmol/L)	Mean value glucose (mmol/L)	CV% (95% confidence interval)
Primary Health Care	51	0	6,0 – 8,5	7,4	3,5 (3,0 – 4,3)

*The given numbers of results (n) are counted before exclusion of outliers. Mean and CV are calculated after exclusion of outliers.

Discussion, repeatability and reproducibility achieved by three primary care centres
As argued for in chapter 2, the precision of glucose meters designed for monitoring blood glucose should give a CV below 5%. For glucose concentrations >7 mmol/L at centre B the CV was 5,3%, and slightly over the quality goal. However, the 95% confidence interval shows that the result is not significantly >5%. The repeatability CV assessed as a whole is approximately 4,5%, and the repeatability must be considered as good.
The reproducibility achieved with the internal quality control solution was good.

5.4. Evaluation of user-friendliness

5.4.1. Questionnaire to the evaluators

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.

At the end of the evaluation period, each user filled in a questionnaire about the user friendliness of Contour. The questionnaire and the expressed opinions are presented in Table 13 to 16. The first column shows what is up for consideration. The second column shows the rating by the users at the four evaluation sites. Table 13, and ratings marked with grey color in table 14, 15 and 16, are filled in by SKUP and the biomedical laboratory scientist in Moss. The third to fifth column show the rating options. The cells with the overall ratings from all four evaluating sites are marked by thicker frames and bold text. The last row in each table summarises the rating in the table. The total rating is an overall assessment of the described property, and not necessarily the arithmetic mean of the rating in the row. Consequently, a single poor rating can justify an overall poor rating, if this property seriously influences on the user-friendliness of the system. Poor ratings are marked with an asterisk and will always be followed by an explanation below the table.

Table 13. Assessment of the information in the manual / insert

Information in manual / insert about:	**Ratings**	**Overall rating**		
		0 point	**1 point**	**2 point**
Table of contents	2	Un-satisfactory	Less satisfactory	**Satisfactory**
Preparations / Pre-analytic procedure	2	Un-satisfactory	Less satisfactory	**Satisfactory**
Specimen collection	2	Un-satisfactory	Less satisfactory	**Satisfactory**
Measurement / reading	2	Un-satisfactory	Less satisfactory	**Satisfactory**
Measurement principle	2	Un-satisfactory	Less satisfactory	**Satisfactory**
Sources of error	2	Un-satisfactory	Less satisfactory	**Satisfactory**
Fault-tracing/Troubleshooting	2	Un-satisfactory	Less satisfactory	**Satisfactory**
Index	2	Un-satisfactory	Less satisfactory	**Satisfactory**
Readability / clarity of presentation	2	Un-satisfactory	Less satisfactory	**Satisfactory**
Available insert in Danish, Norwegian, Swedish	2	Un-satisfactory	Less satisfactory	**Satisfactory**
Others comments about information in the manual / insert (please specify)	-	Un-satisfactory	Less satisfactory	Satisfactory
Rating for the information in the manual				**Satisfactory**

Table 13 is filled in only by the biochemical laboratory scientist.

Table 14. Assessment of time factors

Time factors	**Ratings**	**Overall rating**		
		0 point	**1 point**	**2 point**
Preparations / Pre-analytical time	2,2,2,2	>10 min	6 to 10 min.	**≤6 min**.
Analytic time	2	>20 min	10 to 20 min.	**≤10 min**.
Demands to training	2,2,2,2	days	>2 hours	**0 — 2 hours**
Stability of test, unopened, (no/package)	2	≤3 months	>3 — 5 months	**≥5 months**
Stability of test, opened, (no/package)	2	≤3 months	>3 — 5 months	**≥5 months**
Other comments about time factors (please specify)	-,-,-,-	Un-satisfactory	Less satisfactory	Satisfactory
Rating of time factors				**Satisfactory**

Table 15. Assessment of quality control possibilities

Quality Control	**Ratings**	**Overall rating**		
		0 point	**1 point**	**2 point**
Internal quality control	2,2,2,2	Un-satisfactory	Less satisfactory	**Satisfactory**
External quality control	2	Un-satisfactory	Less satisfactory	**Satisfactory**
Stability of quality control material, unopened	2	≤3 months	>3 — 5 months	**≥5 months**
Stability of quality control material, opened	2	<1 day	<1 week	**≥1 week**
Storage conditions for quality control materials	2		–20°C	**+2 — +30°C**
Other comments about quality control (please specify)	-,-,-,-	Un-satisfactory	Less satisfactory	Satisfactory
Rating of quality control				**Satisfactory**

Table 16. Assessment of the operation facilities

Operation facilities	**Rating**	**Overall rating**		
		0 point	**1 point**	**2 point**
Content of the test kit. Complete?	2,2,2,2	Un-satisfactory	Less satisfactory	**Satisfactory**
Preparations /pre-analytical procedures	2,2,2,2	Un-satisfactory	Less satisfactory	**Satisfactory**
Application of specimen	2,2,2,2	Un-satisfactory	Less satisfactory	**Satisfactory**
Specimen volume	2,2,2,2	Un-satisfactory	Less satisfactory	**Satisfactory**
Number of procedure step	2,2,2,2	Un-satisfactory	Less satisfactory	**Satisfactory**
Ergonomics of the instrument and / or the test devices	1*,2,2,2	Un-satisfactory	Less satisfactory	**Satisfactory**
Reading / Interpretation of the test result	2,2,2,2	Very difficult	Difficult	**Easy**
Sources of errors	2,2,2,2	Un-satisfactory	Less satisfactory	**Satisfactory**
Cleaning/maintenance	2,2,2,2	Un-satisfactory	Less satisfactory	**Satisfactory**
Hygiene, when using the test	2,1**,2,2	Un-satisfactory	Less satisfactory	**Satisfactory**
Stability of the test, unopened	2		–20°C	**+2 — +30°C**
Environmental requirements, waste handling	2,2,2,2	Poison	Sorted waste	**No precautions**
Educational requirements	2	Laboratory education	Laboratory course	**No special education**
Size and weight of package	2,2,2,2	Un-satisfactory	Less satisfactory	**Satisfactory**
Other comments about operation facilities (please specify)	-,-,-,-	Un-satisfactory	Less satisfactory	Satisfactory
Rating of operation				**Satisfactory**

Comments:
*When inserting the test strip into the meter, it feels like there is some resistance in the gap.
**Blood can be spilled when removing the used test strip from the meter.

5.4.2. Assessment of the user-friendliness

The information in the manual or insert was assessed as satisfactory. The users also thought that the time factors and quality control possibilities, as well as the operating facilities, were satisfactory. The evaluators thought that the Contour device was user-friendly.

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.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.
6. www.skup.nu: Reports and summaries from evaluations under the direction of SKUP.
7. Alfhei K, *"Vellykket landskonferanse i NOKLUS"*. Tidsskrift for den Norske Legeforening 2008; **128**: p. 2636.
8. National Institute of Standards and Technology, Certificate of Analysis, Standard Reference Material® 965a, Glucose in Frozen Human Serum
9. 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.
10. Christensen, N.G, Monsen G, Sandberg S, *Utprøving av analyseinstrumenter*. 1997: Alma Mater Forlag.
11. ISO/IEC Guide 99:2007, International vocabulary of metrology (VIM) – Basic and general concepts and associated terms, 3rd edition, JCGM 200:2008.
12. Burnett RW, "*Accurate Estimation of Standard Deviations for Quantitative Methods Used in Clinical Chemistry*". Clinical Chemistry 1975; **21** (13): 1935 – 1938.
13. 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.
14. Fraser, C.G, Biological variation: *From principles to practice*. 2006. Chapter 1 "*The Nature of Biological Variation*". AACC Press. ISBN 1-890883-49-2.
15. Westgard JO, Groth T, de Verdier C-H. *Principles for developing improved quality control procedures*. Scand J Clin Lab Invest 1984; 44 suppl. 172:19-41.
16. Krutchkoff, R. G, *Classical and inverse Regression Methods of Calibration*. Technometrics, Vol. 9, No. 3: 425-439
17. Tellinghuisen, J, *Inverse vs. classical calibration for small data sets*. Fresenius J. Anal. Chem. (2000) 368:585-588.

Attachments

1. Facts about the instrument (in Norwegian), Fakta om instrumentet
2. Raw data glucose, internal quality control (Autonorm), the comparison method
3. Raw data glucose, results from the comparison method
4. Raw data glucose, internal quality control, Contour
5. Raw data glucose, Contour results under standardised and optimal conditions
6. Raw data hematocrit
7. Raw data glucose, Contour results from three primary health care centres
8. "SKUP-info". Summary for primary health care (in Norwegian)
9. List of evaluations organised by SKUP
10. Comments from Bayer AS

Attachments with raw data are included in the report to Bayer only.

Fakta om instrumentet

a) Navn på instrument	Contour
Fysiske dimensjoner	bredde: 57 dybde: 19 høyde: 77 mm
Produsent	Bayer Consumer Care AG Postfach 4002 Basel, Switzerland
Forhandler	Danmark: Bayer A/S Diabetes Care Postboks 2090 DK-2800 Kgs. Lyngby
	Norge: Bayer AS Diabetes Care Postboks 14 N-0212 Oslo
	Sverige: Bayer AB Diabetes Care Box 606 S-16929 Solna

b) Analysemeny, prøvemateriale og analysevolum

Komponent	Prøvemateriale	Analysevolum
Glukose	Fullblod	0,6 µL

c)Analyseprinsipp

Komponent: Glukose
Analyseprinsippet er basert på måling av elektrisk strøm, forårsaket av reaksjonen mellom glukose og reagensene på teststrimmelen. FAD-glukosedehydrogenase oksiderer glukose til glukonolakton. Elektroner fra glukose overføres til mediatoren ferricyanid, som videreleverer elektronene til elektroden. Strømmen som genereres er proporsjonal med mengde glukose i prøven.

d) Analyseområde

Komponent	Analyseområde	Benevning
Glukose	0,6 – 33,3	mmol/L

e) Tid for analysering pr. komponent (angis eksakt)

Komponent	Preanalysetid (med forklaring)	Analysetid
Glukose	ca. 1 minutt: Klargjøre stikkeredskap og apparat, ta en kapillær blodprøve, tørke vekk første dråpe.	5 sekunder

f) Kalibrering

Mulighet for kalibrering	❑ Ja x Nei
Hvor ofte anbefales kalibrering?	Apparatet kalibreres automatisk når man setter inn en blodsukkerstrimmel.
Antall standarder	-
Hvem skal utføre kalibrering	-

g) Anbefalt vedlikehold

Hva gjøres	Hvor ofte
Rengjøring av apparatets utside med en fuktig klut som ikke loer, og et mildt rengjøringsmiddel/desinfiseringsmiddel (for eksempel 1:9 klorløsning). Tørkes med tørr klut.	Ved behov

h) Kontrollmateriale

Finnes det kontrollmateriale fra leverandør eller andre? Bayer Contour kontrolløsning i normalt, lavt eller høyt nivå.

i) Markedsføring

I hvilke land er instrumentet markedsført?	x Skandinavia x Europa x Globalt
Når kom instrumentet på det Skandinaviske markedet?	Sommeren/høsten 2006
Når ble instrumentet CE-godkjent?	2006

j) Språk

Hvilke skandinaviske språk er manualen på? x Dansk x Norsk x Svensk

k) Minne

Hvor stor lagringskapasitet har instrumentet og hva lagres?

480 måleresultater med klokkeslett og dato

Er der mulighet for pasientidentifikasjon? ❑ Ja x Nei
Hvis ja, beskriv dette:

a) Navn på instrument	Contour

l) Strømforsyning

El-nett tilkobling	❑ Ja x Nei
Batteri	x Ja ❑ Nei
Hvis ja, hvilken type og hvor mange batteri	To 3V litiumbatterier (DL2032 eller CR2032)

m) Elektronisk kommunikasjon

Kan printer kobles til instrumentet?	❑ Ja x Nei
Kan barkodeleser kobles til instrumentet?	❑ Ja x Nei
Interface	x Ja ❑ Nei
Hvis ja, hvilken utgang kreves?	Bayer leverer USB-kabel og CD med driver. Serieport kan tilbys.
Kommunikasjonsmåte	x enveis ❑ toveis

n) Standarder og kontroller

	Standard	Kontroll
Navn		Contour kontrolløsning, 3 nivå
Volum		2,5 mL
Holdbarhet uåpnet		Til utløpsdato notert på flaskeetiketten
Holdbarhet åpnet		6 mnd
Evt. kommentarer:		

o) Reagenser

Komponent	Tid og temperatur, uåpnet	Tid og temperatur, åpnet
Contour blodsukkerstrimler	24 mnd fra produksjonsdato, +15 - +30 °C	6 mnd, +15 - +30 °C
Evt. kommentarer:		

p) Tilleggsopplysninger

Attachment 2

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

Date	Res. Autonorm 1 glucose, mmol/L	Res. Autonorm 2 glucose, mmol/L
31.08.09	3,46	15,07
31.08.09	3,50	15,35
01.09.09	3,45	14,99
01.09.09	3,48	15,26
02.09.09	3,42	14,99
02.09.09	3,52	15,26

Attachment 4

Raw data glucose, internal quality control, Contour

Contour control	Lot-no	Expiry	Glucose level mmol/L
normal	1741098	2010-09	6,0 – 8,3

Contour Control normal, analysed on the biomedical laboratory scientist's meter

Date	Lot 9BC3D01, glucose mmol/L	Lot 9BC3D06, glucose mmol/L	Lot 9BC3C06, glucose mmol/L
01.apr	7,3	7,4	7,6
02.apr	7,3	7,7	7,6
14.apr	7,4	7,8	7,9
15.apr	7,8	7,3	7,8
16.apr	7,6	7,7	7,8
20.apr	7,3	7,7	7,7
21.apr	7,7	7,9	7,6
22.apr	7,7	7,8	7,9
27.apr	7,7	7,6	7,8
28.apr	7,4	7,7	7,7
05.mai	7,5	7,8	7,6
06.mai	7,6	7,8	7,8
19.mai	7,7	7,8	7,6
20.mai	7,4	7,7	7,7
25.mai	7,7	7,7	7,7
28.mai	7,6	7,7	7,8
19.jun	7,4	7,3	

Contour Control normal, analysed at primary health care centre A

Date	Lot 9BC3D01, glucose mmol/L
24.apr	7,4
30.apr	7,3
04.mai	7,2
05.mai	7,3
07.mai	7,1
08.mai	7,1
11.mai	7,3
15.mai	7,4
18.mai	7,3
19.mai	7,4
02.jun	6,9
04.jun	7,3
05.jun	7,3

Contour Control normal, analysed at primary health care centre B

Date	Lot 9BC3C06, glucose mmol/L
24.apr	7,3
27.apr	7,6
29.apr	7,8
30.apr	7,4
04.mai	7,5
05.mai	8
06.mai	7,3
07.mai	7,6
08.mai	7,9
11.mai	7,4
12.mai	7,4
13.mai	7,4
14.mai	6,7
18.mai	7,2
19.mai	7,9
20.mai	7,6
28.mai	7,4
29.mai	7,7
02.jun	7,5
04.jun	7,2

Contour Control normal, analysed at primary health care centre C

Date	Lot 9BC3D06, glucose mmol/L
23.apr	7,7
24.apr	7,3
27.apr	7,7
30.apr	7,6
04.mai	7,7
05.mai	7,3
06.mai	7,4
07.mai	7,6
11.mai	7,3
13.mai	7,4
14.mai	7,7
15.mai	7,4
18.mai	7,3
19.mai	7,5
20.mai	7,7
22.mai	7,8
26.mai	7,9
27.mai	7,1

SKUP-info

Contour blodsukkerapparat fra Bayer HealthCare
Sammendrag fra en utprøving i regi av SKUP

Konklusjon
Presisjonen på Contour var god, med en CV på ca 4 %. Contour ga nøyaktige måleresultat. Internasjonale kvalitetskrav fra ISO 15197, med et avvik på mindre enn ± 20 % fra en anerkjent glukosemetode, ble oppfylt. Den totale målefeil var ca. 10 %. Hematokrit så ikke ut til å påvirke glukosemålingene.

Contour er beregnet til måling av blodsukker i kapillærblod, både av personer med diabetes og av helsepersonell. Systemet er produsert av Bayer HealthCare og består av Contour apparat og Contour teststrimmel. Det kreves 0,6 µL blod til hver måling. Målingen tar 5 sekunder. Apparatet trenger ikke kodes. Contour har minnekapasitet til å lagre 480 resultat.

Utprøvingen ble utført under optimale betingelser av laboratorieutdannet personale i et sykehuslaboratorium, og på tre norske legekontor. Det ble tatt prøver av 98 personer på sykehuslaboratoriet, og på de tre legekontorene ble det tatt prøver av til sammen 119 pasienter.

Resultater
Presisjonen på Contour var god. CV var ca. 4 %, både når målingene ble utført av laboratorieutdannet personale, og når brukerne på tre legekontor gjorde målinger på Contour. For glukoseverdier < 10 mmol/L samsvarte resultatene på Contour med resultatene på sammenligningsmetoden. For glukoseverdier over 10 mmol/L ga Contour ca. 0,5 mmol/L for lave verdier. Kvalitetsmålet fra ISO 15197, som tillater avvik opp til ± 20 % fra en anerkjent metode for måling av glukose, ble oppfylt. Den totale målefeil ble beregnet til ca. 10 %. Hematokrit i området 27 — 49 % så ikke ut til å påvirke glukosemålingene på Contour.

Brukervennlighet
Brukerne mente at Contour-systemet var enkelt i bruk, og de var fornøyde med apparatet.

Tilleggsinformasjon
En fullstendig rapport fra utprøvingen av Contour, SKUP/2009/75, finnes på SKUPs nettside, www.skup.nu. Opplysninger om pris fås ved å kontakte leverandør. Laboratoriekonsulentene i NOKLUS 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

SKUP evaluations from number 51 and further

Evaluation no.	Component	Instrument/testkit	Producer
SKUP/2009/75	Glucose	Contour	Bayer HealthCare
SKUP/2009/74	Glucose[1]	Accu-Chek Mobile	Roche Diagnostic
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 Development 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

*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

SKUP evaluations from number 1 — 50

Evaluation no.	Component	Instrument/test kit	Producer
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
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

For comments regarding the evaluations, please see the indications on the first page

Attachment 10

Comments from Bayer AS

06.09.2009

Bayer reviewed the draft version of the report and has the following comments:

Bayer only proposed some minor changes to the draft protocol from SKUP. All relevant information and requirements regarding the start-up of the three evaluation sites was received in a clear and timely fashion. Once the evaluation had started Bayer did not have any contact with the sites.

The results of this study confirm our internal performance data on file and the customer feedback from market. Bayer's Contour delivers excellent precision and accuracy for our Point of Care users, all provided in a user-friendly and easy to use format. Our hematocrit sensor and built in hematocrit correction is useful for these settings and works well.

Bayer would like to take the opportunity to thank the SKUP organization for the excellent service and professionalism provided throughout the evaluation of Bayer's Contour.

Torstein Myhre
Nordic Bayer HealthCare Representative

Bayer HealthCare
Diabetes Care

Torstein Myhre
Country Division Head-Nordic

Bayer AS
Drammensveien 147b
Postboks 14, 0212 Oslo
Phone: +47 241 11 806
Cellphone: +47 915 25 946

E-mail: torstein.myhre.tm@bayer.no
URL: www.bayerdiabetes.no