Quo-Test™ A1c

A system for measurement of B-Haemoglobin A1c
manufactured by Quotient Diagnostics Ltd

Report from an evaluation
under optimal conditions in a hospital laboratory
and in primary health care
organised by SKUP

Evaluated at the request of Triolab, Denmark

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SKUP/2012/91

The report was written by SKUP, 2011.
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The organisation of SKUP

Scandinavian evaluation of laboratory equipment for primary health care, *SKUP*, is a co-operative commitment of NOKLUS[1] in Norway, 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 organizing 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. In addition, SKUP reports are published at www.skup.dk, where they are rated according to the national Danish quality demands for near patient instruments used in primary health care. SKUP as an organisation has no responsibility for www.skup.dk.

[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. SKUP in Denmark reports to DAK-E (Danish Quality Unit of General Practice), an organisation that is supported by KIF (Foundation for Quality and Informatics) and Faglig udvalg (Professional Committee), which both are supported by DR (The 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).

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A detailed list of previous SKUP evaluations is included in the attachments.
Attachments with raw data are only included in the copy to Triolab.

1. Summary

Triolab, Denmark turned to SKUP for an evaluation of Quo-Test HbA1c in September 2010. The evaluation was performed in the Department of Clinical Biochemistry, Hillerød Hospital and in two primary health care centres in Farum and Birkerød, respectively in the period January to May 2011.

The aim of the evaluation

- To examine the repeatability, trueness and accuracy of Quo-Test in a hospital laboratory achieved with capillary and venous samples from 100 individuals
- To examine the repeatability, trueness and accuracy of Quo-Test in two primary health care centres achieved with capillary samples from 40 patients in each of the two centres
- To evaluate the performance of control materials on the Quo-Test instrument
- To evaluate the user-friendliness of Quo-Test in a hospital laboratory and in two primary health care centres

Materials and methods
Venous whole blood samples and capillary samples from 102 individuals were examined in the hospital. Capillary samples from 84 patients were tested in primary health care centres. Bias and repeatability of Quo-Test were calculated from duplicate results for three levels of HbA1c. Three lots of test cartridges were used. All HbA1c results in this evaluation are presented in DCCT % units.

Results
In both the hospital laboratory and in the two primary health care centres, for capillary as well as venous samples, 95% of the single results had a deviation of less than ±10% from the comparison method.
For capillary samples, a bias within ±4,0% was reached in both hospital laboratory and primary health care centres. For the venous samples at the hospital laboratory the bias was within ±4,0% for HbA1c levels above 5,6%, and -4,6 % for samples with lower HbA1c values.
At the hospital laboratory the repeatability varied between 2,0 and 5,2% for capillary samples and between 1,6% and 4,6% for venous samples. For capillary HbA1c levels above 5,6% and venous HbA1c levels above 6,8% the repeatability was less than 4,0%. At the two primary health care centres the repeatability varied between 3,3% and 5,1%. For HbA1c levels above 6,1% in one primary health care centre and above 4,7% in the other primary health care centre, the repeatability was less than 4,0%.
The percentage of technical errors was 2,2%.
The user-friendliness was satisfying, based on the manual and inserts, the time factors of both measurement and preparation, performing of internal and external quality control and for operational ease of use in both primary health care centres and hospital laboratory.

Conclusion
In the hospital laboratory: Quo-Test fulfilled the analytical quality goal for accuracy with both capillary and venous sample. The bias goal (within ±4,0%) was fulfilled with capillary samples. For venous results below 5,6% the goal was not fulfilled, but above this level the trueness was satisfactory. The goal for repeatability was fulfilled with venous and capillary sample results above 5,6% and 6,8%, respectively. For HbA1c below these levels the goal for repeatability was not fulfilled.
In the primary health care centres: The quality goals for accuracy and bias were fulfilled in both centres. One primary healthcare centre fulfilled the goal of repeatability <4,0 CV% for all samples; the other fulfilled the goal for HbA1c levels above 6,1%.
The error frequency was 2,2% and just above the goal of ≤2,0%.
The user-friendliness was satisfactory.

Comments from the requesting company
A letter with comments and additional information from the manufacturer is attached to the report.

2. Abbreviations

ADA	American Diabetes Association
CI	Confidence Interval
C-NPU	Committee of Nomenclature, Properties and Units
CV	Coefficient of Variation
CV_a	The analytical imprecision expressed as the coefficient of variation
CV_{bw}	The intra-individual biological variation, biological variation within individuals
CV_{bb}	The inter-individual biological variation, biological variation between individuals
DAK-E	Danish Quality Unit of General Practice
DCCT	Diabetes Control and Complications Trial
DEKS	Danish Institute of External Quality Assurance for Laboratories in Health Care
DSKB	Dansk Selskab for Klinisk Biokemi (Danish Society for Clinical Biochemistry)
eAG	estimated Average Glucose
EQA	External Quality Assessment
EQUALIS	External quality assurance in laboratory medicine in Sweden
HPLC	high-performance liquid chromatography
HbA1c	B-Haemoglobin A1c
IFCC	International Federation of Clinical Chemistry and Laboratory Medicine
IUPAC	International Union of Pure and Applied Chemistry
JDS/JSCC	Japanese Diabetes Society/Japanese Society for Clinical Chemistry. Calibration methods for HbA1c used in Japan
NGSP	National Glycohaemoglobin Standardization Program
NOKLUS	Norwegian Quality Improvement of Primary Care Laboratories
Quo-Test	Quo-Test™ A1c
SD	Standard Deviation
SKUP	Scandinavian evaluation of laboratory equipment for primary health care
Swedac	Swedish Board for Accreditation and Conformity Assessment
TE	Total Error
UKPDS	UK Prospective Diabetes Study

3. Quality goals

To qualify for an overall good assessment in a SKUP evaluation, the measuring system must show satisfactory analytical quality as well as satisfactory user-friendliness.
There are no generally recognised analytical quality goals for HbA1c-determinations. Various ways of setting goals for analytical quality are presented below.

3.1. Analytical quality goals

3.1.1. *Analytical quality goals based on biological variation*
The HbA1c value describes an average of the glycaemic level over the last two months. However, the within-subject biological variation might not be the same for healthy individuals and diabetics. If the biological variation is used as goal, it is recommended that analytical imprecision (CV_a) should be less than half of the biological variation within healthy individuals (CV_{bw}) [1]. The optimal quality goal for bias is $\leq 1/4\sqrt{CV_{bb}^2 + CV_{bw}^2}$ where CV_{bb} is the biological inter-individual variation between healthy individuals. Ricos [2], referring to sources from 1985 - 2002, claims the CV_{bw} to be 3,4%, while later publications give figures below 3% [3].

Permitted total error (TE) is a function of imprecision and bias. The total error (TE) should be $\leq \pm$ [| bias | + 1,65 x CV]. If Ricos figures [3] are taken into accordance, the quality goal for imprecision is ≤1,7%, Bias ≤1,5% and total error (TE) is ≤4,3%.

3.1.2. *Analytical quality goals based on recommendations from professionals/experts*
The American Diabetes Association (ADA) recommends an intralaboratory CV <2% and an interlaboratory CV <3.5% for HbA1c. At least two control materials with different mean should be analyzed as an independent measure of assay performance [4].

The National Glycohaemoglobin Standardization Program (NGSP) in the USA recommends that the between-day CV for HbA1c must be less than 4%, and that 95% of the results must be within ±0,75 HbA1c-percent for the purpose of methodological comparison with a reference laboratory.

In Norway, in a joint statement 2002, the Endocrinological Association and Clinical Chemistry and Clinical Physiology recommended that suppliers of HbA1c methods should give evidence of a day-to-day variation less than 3%.

The Laboratory Committee under the Professional Committee in Denmark recommends that the CV_a of measuring HbA1c in primary health care should be less than 4%, and that the bias should not exceed 4%. For the HbA1c-instruments in the hospital laboratories, the CV_a as well as bias should be less than 3% [5].

In Sweden the Swedish biochemical society and the External quality assurance in laboratory medicine in Sweden (EQUALIS) have decided on a national quality goal, where the bias should be ≤ 1,5 mmol/mol and the reproducibility ≤2,5 % CV (in IFCC-units) [6].

3.1.3. *Analytical quality goal based on "state-of-the-art"*
Three different studies [7-9] show that CV_a for HbA1c measurement ought to be <3%.

3.1.4. *Quality goals derived from expectations among patients and doctors*

General practitioners in Norway have been asked which analytical quality they need [10].
The median of a wanted within-laboratory analytical imprecision was 2,2 CV%. However, in reality they noticed such small changes in HbA1c concentrations that they assumed there was no imprecision. A majority of the doctors also expected a smaller between-laboratories CV than the measured 3,2%.
Diabetes patients in Norway have also been asked which analytical quality they expect [10]. What change in HbA1c from 9,4% (DCCT) is necessary for a patient to be certain that the change indicates a true (real) improvement or deterioration of their diabetes, i.e. the so-called critical difference. From the answers, the expected analytical imprecision can be calculated, considering the known biological variation, assuming the bias component to be zero and the statistical significance set to 5%. By doing so, the patient-derived quality specification for imprecision was determined to about 3 CV%.

3.1.5. *Other expectations from primary health care*

It is a wish from the Danish general practitioners, that the percentage of "tests wasted" caused by technical errors should not exceed 2%.

3.2. Evaluation of user-friendlines

The evaluation of user-friendliness is carried out by asking each of the evaluating persons to fill in a questionnaire.

The questionnaire divides the user-friendliness into four sub-areas:

- Rating of information in manuals and inserts
- Rating of time factors of both measurement and preparation
- Rating of performing internal and external quality control
- Rating of operation facilities. Is the system easy to handle?

Evaluation of user-friendliness is graded as satisfactory, intermediate or unsatisfactory, also depicted by the colours green, yellow, and red.
To achieve the overall rating "satisfactory", the tested equipment must reach the total rating of "satisfactory" in all four sub-areas of characteristics mentioned above.

3.3. SKUP's quality goals in this evaluation

Based on the discussion about quality goals above, SKUP has decided to assess the results from the evaluation of the Quo-Test™ A1c (Quo-Test) against the quality goals in table 1.

Table 1. Quality goals in the evaluation of Quo-Test

	Goal
Imprecision (CV)	≤4%
Bias (systematic deviation from the Comparison Method)	≤4%
Inaccuracy (allowable deviation)	≤±10%
Fraction of technical errors	≤2%
User-friendliness	satisfactory

In this evaluation the numerical values of the analytical quality goals are based on HbA1c results in the unit % standardised according to Diabetes Control and Complications Trial (DCCT).

4. Materials and methods

The purpose of HbA1c measurements has been monitoring of the treatment of diabetes, it might become part of the diagnosing diabetes as well.

Diabetes Control and Complications Trial (DCCT) [11] and the UK Prospective Diabetes Study (UKPDS) [12] demonstrated the clinical impact of lowering the blood glucose level in persons with Diabetes mellitus type 1 and type 2, respectably. The standardisation used in both these studies has been kept in the NGSP. The idea is that results today can be directly compared to results and clinical outcomes in the above studies where relationships to mean blood glucose and risk for vascular complications have been established. The purpose of the NGSP is to standardize glycated haemoglobin test results so that clinical laboratory results are comparable to those reported in the DCCT.

4.1. Definition of HbA1c

HbA1c was earlier defined as the chromatographic fraction of haemoglobin glycated to A1c of the total amount of haemoglobin. The measurement results have therefore been procedure specific and varied with the chromatographic system used. However, other components have been reported to influence these measurements [13].

In the international hierarchy of methods a reference measurement procedures has the highest rank. For measurement of HbA1c two references, measurement procedures have been approved by IFCC [13]. Results from the earlier systems for standardization of HbA1c measurements, that is the NGSP (USA), and the JDS/JSCC standardisation (Japan) [14] and Mono S (Sweden), have been compared with the IFCC reference methods. The linear relations between the different standardisation procedures are described by established master equations [13,14].

The International Federation of Clinical Chemistry and Laboratory Medicine (IFCC) and the International Union of Pure and Applied Chemistry (IUPAC) work in a joint Committee on Nomenclature, Properties and Units (C-NPU). Descriptions of clinical laboratory quantities are listed in the ”NPU database” [15]. The quantities being measured by HbA1c-tests are described in table 2. The description is valid for all procedures traceable to the IFCC reference measurement procedure.

Table 2. Name, code and unit for HbA1c tests according to C-NPU

NPU code	Full name of test according to NPU	Short name	Unit
NPU27300	Hb beta chain(B)—N-(1-deoxyfructos-1-yl)Hb beta chain; substance fraction = ?	Haemoglobin A1c (IFCC);Hb(B)	mmol/mol
NPU03835*	Hb(Fe; B)—Haemoglobin A1c(Fe); substance fraction = ?	Haemoglobin A1c;Hb(B)	unit 1 (fraction)

*The code NPU03835 is used in Denmark for HbA1c values given as fractions. For DCCT values given in DCCT % unit the local code RHB00001 is used in the Copenhagen region (RegionH).

In this report HbA1c is used as the short name and the results are presented in % (DCCT) units.

4.1.1. *Traceability of HbA1c results*

According to the 2010 international consensus agreement [16], all HbA1c results should be traceable to the IFCC reference methods and be reported in both IFCC units (mmol/mol) and in DCCT units (%). Results from both the comparison method, Tosoh G7 in Hillerød, and the evaluated method, Quo-Test, are traceable to the IFCC reference method.

4.1.2. *Differences in Scandinavia:*

Beginning in 2011 Sweden now uses the IFCC values [6]. Norway uses the NGSP (DCCT) values. Danish Society for Clinical Biochemistry has published recommendation for reporting from Danish laboratories [17]. Most laboratories in Denmark give three results for each measurement of HbA1c: the HbA1c (DCCT), the HbA1c (IFCC) and the estimated Average Glucose (eAG). Relations between HbA1c (IFCC) mmol/mol, HbA1c % (DCCT), and eAG mmol/l are shown in table 3 [17].

Table 3. Conversion table for between differently standardised HbA1c values

HbA_{1c}(IFCC) mmol/mol	**HbA_{1c}(DCCT) %**	**eAG mmol/l**
20	4,0	3,8
31	5,0	5,4
42	6,0	7,0
48	**6,5**	7,7
53	**7,0**	8,5
58	7,5	9,3
64	8,0	10,1
75	9,0	11,7
86	10,0	13,3

The numbers in bold are the two suggested cut-off limits for treatment. ADA and the UKPDS recommend treating new diabetics at the level HbA1c 7,0% (DCCT) (13) whereas the European Association for the Study of Diabetes (EASD) recommends, that the HbA1c goal for treatment of the diabetics is 6,5% (DCCT) or less.

4.2. The Quo-Test™ A1c system

The Quo-Test™ A1c system is a near patient system intended for use by health care personnel in primary health care, hospital clinics, etc. The instrument can present the results according to several different standards: NGSP, JDS, and Mono S. Regardless of the selected reporting mode, the instrument will also report the IFCC result in mmol/mol units.

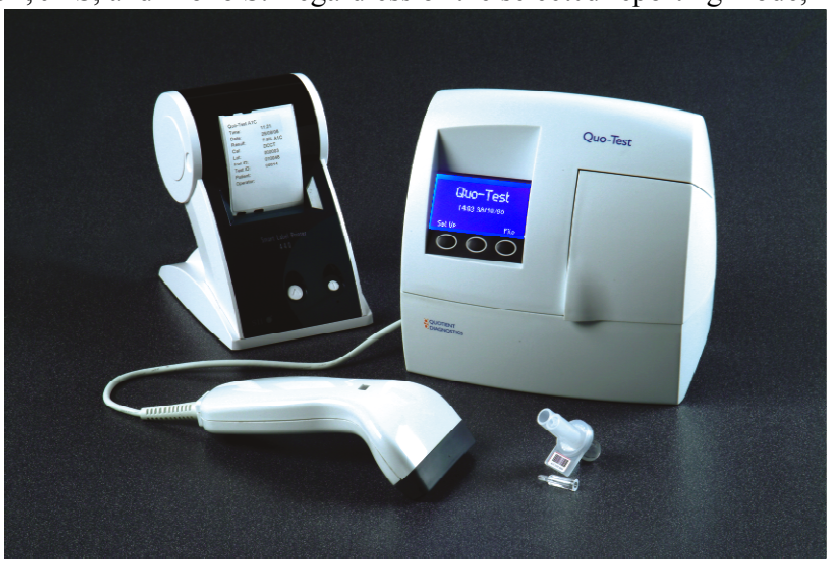

Figure 1: The Quo-Test system with the Analyser including the barcode reader and a printer, and the Test Cartridges with the blood collector

Quo-Test is delivered with a barcode reader enabling optional barcode reading for patient ID and/or operator ID. The barcode reader is necessary for reading calibration information on each lot of test cartridges and when analysing a control. A printer is sold separately.
The Quo-Test system consists of three parts: The Quo-Test Analyser, the Quo-Test HbA1c Test Cartridges including blood collectors and the Quo-Test Quality Control set, consisting of a high and a low freeze-dried control, used to check the analyser.
The system requires a blood amount of 4 µL. A blood collector supplied with the test cartridges collects the blood. The instrument can store up to 7000 results. For more information on the instrument, please see attachment 1.

Analysing a patient sample
A short version of the procedure for analysing capillary blood on Quo-Test is shown below in figure 2. The illustrations were found in the Danish version of the instrument guide supplied by Triolab [18]. Capillary whole blood as well as venous EDTA whole blood may be used.

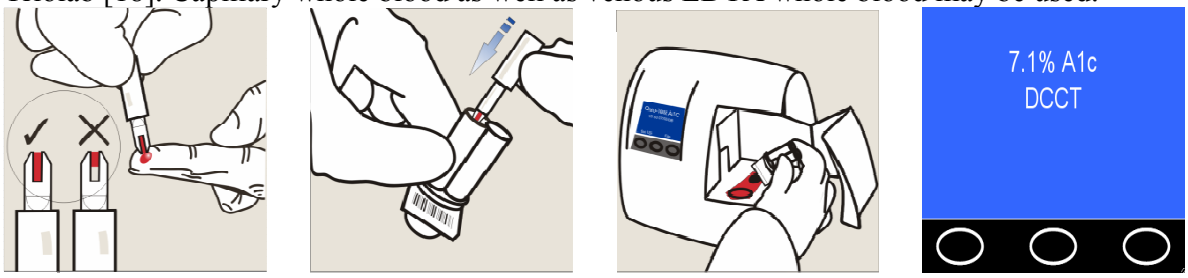

Figure 2: Analysing a patient sample. Please see attachment 2 for a full guide to sampling (Danish)

1. Capillary blood is drawn from a fingertip and 4 µl is collected with the blood collector
2. The blood collector is placed in the test cartridge, placed in the analyser, and locked into place by pulling the slide
3. After closing the analyser the procedure is automatic and the result is displayed on-screen after 4 minutes

Analysing a Quotient control
The Quo-Test Quality Control set should be analysed once a month, when new lots are taken into use and if a measurement is suspected to be wrong. Both levels should always be tested. Before a control is analysed the barcode is scanned. The scan brings the instrument in "high level control mode" or "low level control mode". Otherwise, analysis of a control sample is similar to analysing a patient sample. When the control analysis is done the result of the test is shown on-screen with a message specifying that the control level is either within or out of range.

Measuring principle
Quo-Test uses boronate affinity fluorescence quenching to separate the glycated haemoglobin fraction from the non-glycated haemoglobin fraction. In short, the HbA1c binds to the boronate conjugate and this binding quenches the fluorescence. A fluorimeter within the QuoTest analyzer is used to measure the percentage fluorescence quenching, this being a function of HbA1c concentration. The fluorimeter is also used to determine the total Hb; the initiate drop in fluorescence signal, prior to the HbA1c binding to the boronate conjugate, being a function of total Hb concentration. A secondary photometric measurement is also made to determine the reagent concentration, this measurement being used to make a small adjustment to the final %HbA1c result.
Quo-Test reports HbA1c results from 2 to 17% (DCCT). Results below 2% (DCCT) are given as "Resultat lavt" and results above 17% (DCCT) as "Resultat højt" in the Danish version of the instrument, translated to "result low" and "result high", respectively, in English.

4.2.1 Product information
Quo-Test™ A1c is manufactured by Quotient Diagnostics Limited.
Technical data from the manufacturer is shown in table 4.
For names of suppliers in the Scandinavian countries and more details about Quo-Test, see attachment 1.

Table 4. Technical data from Quotient

Technical data for Quo-Test	
Optimal operating temperature	18-32°C
Humidity	10-80%
Sample material	Capillary whole blood or venous EDTA whole blood
Sample volume	4 µL
Measuring time	4 minutes
Measuring range	2,0-17,0% (DCCT)
Hematocrit	18,3-62,2%
Storage capacity	7000 results
Electrical power supply	100-240 VAC, 50-60 Hz, 30 W
Operating time with battery	Not applicable
Dimensions	205 mm x 135 mm x 205 mm
Weight	1310 g

The following instruments and reagents were used in the evaluation:
Quo-Test Analysers: 010299 (instrument 1)
010300 (instrument 2)
010371 (instrument 3)
010297 (instrument 4) back-up instrument

Printers:	4409AA03245	
	4409AA03151	
	4409AA07547	
	4409AA00944	back-up printer
Test cartridges:	010041 (lot 41)	expiration date: 2011-06
	010042 (lot 42)	expiration date: 2011-06
	010046 (lot 46)	expiration date: 2011-07
Quo-Test Quality Control:	Quotient does specify range on the controls in DCCT, IFCC and JDS concentrations	
	CS07 5,8—8,2% (DCCT)	expiration date: 2011-08
	CS09 11,2—14,8% (DCCT)	expiration date: 2011-12

4.2.1. *Manufacturer of Quo-Test*
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4.2.2. *Suppliers in the Scandinavian countries*
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4.3. The selected comparison method

The selected 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.

4.3.1. *The selected comparison method in this evaluation*

The routine method at the Department of Clinical Biochemistry at Hillerød Hospital, Tosoh G7 from Tosoh Corporation, was selected as the comparison method in this evaluation. The method is hereafter called "the comparison method".

Instrument	Three Tosoh G7 instruments, below called Tosoh 1/2/3. Tosoh 2 was used as a back-up for the other instruments.
Calibration and traceability	A two point calibration using high and low calibrators from Danish Institute of External Quality Assurance for Laboratories in Health Care (DEKS) with assigned IFCC values converted into DCCT % values.
External quality Assessment (EQA)	The Department of Clinical Biochemistry, participates in the Labquality survey number 3044 sent out five times every year.
Internal quality control	Every day three controls are analysed. A control from DEKS with an assigned value and two Bio-Rad controls with a range in the normal and high values.
Goals for Dept. of Clinical Biochemistry, Hillerød	A maximum difference between instruments of 0,4% (DCCT) is allowed. For the instruments the goals are: CV <2,6%; desired. Bias (in relation to peer group mean) <1,7%; desired. Bias (in relation to peer group mean) < 1,3% optimal.
Samples	Venous whole blood collected in tubes containing EDTA.
Measurement Principle:	The Tosoh G7 from Tosoh Corporation is an HPLC method. A cation exchange nonporous polymer column achieves haemoglobin separation of the various fractions and elution is performed by a step-wise gradient using three citric acid buffers with different salt concentrations and pH. The fractions are measured as absorbance at 415 nm.

4.3.2. *Verification of the comparison method*

The bias and the imprecision of the comparison method instruments in the Department of Clinical Biochemistry were calculated before, under and after the evaluation. The deviation from other Tosoh instruments in the Labquality EQA programme had been <±1% (DCCT) (12 months before the evaluation) and the imprecision had been <2 CV%, 12 months before the evaluation. See table 7 in chapter 6.

Since the start of using DEKS calibrators assigned with values in the unit mmol/mol, the Tosoh HbA1c method group has had a bias in the Labquality EQA program when compared to the results from the European Reference Laboratory for Haemoglobin A1c, in the Netherlands. The reference laboratory uses two Secondary Reference Methods with different analytical principles.

Both SKUP in Denmark and the requesting company were aware of this issue and therefore it was decided to monitor and subsequently correct the results in this evaluation for this bias. The bias correction is seen in section 6.2.1.

4.3.3. *Procedures in the laboratory*
The venous samples were analysed as routine samples for the comparison method, but contrary to the routine procedure, in duplicates and on two different instruments.

4.3.4. *Product information, the comparison method*

Instruments:	Tosoh G7, Tosoh Corporation Serial numbers: 10632903, 11153104, 12356205
Reagent:	Elution buffer HSi Variant No 1: Lots H7-101R to H7-110R, consecutive lot numbers Elution buffer HSi Variant No 2: Lots H7-201R, H7-202R, H7203R Elution buffer HSi Variant No 3: Lots H7-301R to H7-305 R, consecutive lot numbers Haemolysis Reagent & Wash Solution: Lots: 84 A/B, 99 A/B, 11 A/B, 12A/B
Calibration:	Tosoh instrument 1, 2 and 3: 15th June 2010 The following calibrators were used at the calibrations: DEKS, low calibrator: lot 2009.1191, expiry 2017-08, assigned value 5,12% (DCCT) DEKS, high calibrator: lot 2009.1193, expiry 2017-08, assigned value 10,00% (DCCT) Tosoh 1 was also calibrated the 2nd, 3rd and 8th of February 2011. The following calibrators were used at the calibrations: DEKS, low calibrator: lot 2009.3251, expiry 2019-10, assigned value 5,49% (DCCT) DEKS, high calibrator: lot 2009.3253, expiry 2019-10, assigned value 9,50% (DCCT)
Internal quality control:	DEKS control, target 8,11% (DCCT) lot 2007.1432, exp. 2017-08 Bio-Rad 1, lot 33791 (5,5-5,9% (DCCT)), expiry 30th April 2012 Bio-Rad 2, lot 33792 (9,0-9,6% (DCCT)), expiry 30th April 2012

4.4. Planning of the evaluation

4.4.1. *Background for the evaluation*
Triolab, Denmark, applied in 2010 for an evaluation of Quo-Test in both hospital and primary health care centres. SKUP accepted to carry out this evaluation on behalf of Triolab. The Quo-Test system is produced by Quotient. At the start of the evaluation it was not supplied in Scandinavia.

4.4.2. *Meetings, contract, and protocol*
A meeting with participants from Quotient, Triolab and SKUP was held at Hillerød Hospital on the 8th of November 2010. In the meeting, the protocol was discussed and approved. The contract was signed November 2010.

4.4.3. *Blood sampling devices and Collection of samples*
All individuals had two capillary tests performed on Quo-Test using procedures in attachment 2. Two skin punctures, using Mumford Unistik®3 Extra, Gauge 21G (0,81mm), depth 2,0 mm, were made to collect the two samples. The second blood drop was used for analysing on Quo-Test.
Following this, two venous samples (two Greiner 3 mL tubes containing K_3EDTA in one skin perforation) were drawn. The tubes were inverted 8-10 times to ensure thorough mixing. One tube was for analysis on the comparison method, and one was for analysing on Quo-Test.

4.4.4. *Evaluation sites and persons involved*
The hospital evaluation took place in Hillerød Hospital, Department of Clinical Biochemistry.
The primary health care evaluation took place in centres that normally do not use capillary samples to analyse HbA1c.
Primary health care centre 1: Lægehuset Farum Midtpunkt, Farum. This primary health care centre consists of four general practitioners, three nurses and one secretary. All nurses at this centre handle all types of laboratory samples and they all participated in this evaluation.
Primary health care centre 2: Lægerne Mygind, Øgard and Jørgensen, Birkerød. At the primary health care centre, there are three general practitioners and four nurses. The nurses all do laboratory work, but only two of them handled the samples for the evaluation.

Table 5. Persons involved in the evaluation

Place	Person	Title	Task
Hillerød Hospital	Esther A Jensen	Physician	Author of the report Statistical calculations
Hillerød Hospital	Steen Ingemann Hansen	Civil engineer	Responsible for the comparison method
Hillerød Hospital	Doris Nellemann	Biomedical laboratory scientist	Responsible for the comparison method
Hillerød Hospital	Stine Beenfeldt Weber	Cand. Scient.	Hospital evaluation and contact person for primary health care. Co-author of the report
Hillerød Hospital	Inge Lykke Pedersen	Biomedical laboratory scientist	Consultant for primary health care quality
Primary Health Care Centre1	Bettina Søltoft Friis Helle Matzen	Nurses	Primary health care testing
Primary Health Care Centre 2	Stine Thim Nielsen Mariette Kryger	Nurses	Primary health care testing

4.5. The evaluation procedure

4.5.1. *The evaluation model*

The bias and repeatability of the comparison method results was checked. The comparison method results used in the evaluation are adjusted for bias.

The aims of the evaluation in the hospital laboratory and the two primary health care centres were:

- To examine the repeatability and accuracy of Quo-Test in a hospital laboratory achieved with capillary and venous samples from more than 100 individuals
- To examine the repeatability and accuracy of Quo-Test in two primary health care centres. achieved with capillary samples from 40 patients in each of the two primary health care centres
- To evaluate the performance of Quo-Test and DEKS control materials on the Quo-Test instrument
- To evaluate the user-friendliness of Quo-Test in a hospital laboratory and in two primary health care centres

The manufacturer, Quotient, and the supplier, Triolab, requested that the HbA1c results in this evaluation should be presented in DCCT % units.

The capillary samples and the venous EDTA sample from each patient were measured in duplicates using the same Quo-Test instrument and test cartridges with the same lot number. EDTA whole blood samples from the same patients were measured twice with the comparison method. Six HbA1c-measurements were made on each patient in the evaluation.

4.5.2. *Evaluation procedure in the hospital laboratory (standardised and optimal conditions)*
Training

Stine Beenfeldt Weber was trained by Esben Smith and Gert Pynt, Triolab, on the 8th of November 2010. Test samples of capillary blood, venous EDTA blood and control material were analysed using a Quo-Test system at the Department of Clinical Biochemistry, Hillerød Hospital.

Recruitment of patients
Outpatients coming to the hospital to have their HbA1c measured routinely were invited to participate in the hospital evaluation. Participation was voluntary, and verbal consent was considered sufficient. Each patient was included only once. 102 patients agreed to participate.

Handling of samples and measurements, Quo-Test
All individuals had two capillary samples taken and two venous EDTA samples drawn, all according to the procedure in section 4.3.3. For capillary samples, the second blood drop was used.
The samples were analysed in duplicates with Quo-Test, first the two capillary whole blood samples (two skin penetrations), then two venous EDTA whole blood samples (one tube), a total of four measurements on the same day on one Quo-Test instrument for each patient. All measurements on one patient were done using one lot number of test cartridge and one instrument.
Three lot-numbers of Quo-Test test cartridges were used in this evaluation.

Analysing with the comparison method
After the first measurement with the comparison method, the samples were reanalysed on the other comparison method instrument used in the evaluation. The time from blood sampling to analysis to the first measurement was maximum 18 hours. If the sample was not analysed on the same day as collected, it was kept at +4 ^{o}C until analysis the next day.

Comparison method, quality assurance
Please see section 4.3.1.

Quality assurance with Quo-Test
To monitor the quality of measurements on Quo-Test, two control materials from Quotient was analysed in duplicates every day. One control was a high-level control, and one a low-level control. In addition, the DEKS internal control from the comparison method (see section 4.3.4) was analysed in duplicate every day.

Recording of results
All results were registered and signed by the evaluator. If an instrument showed an error code while analysing a sample, a new measurement was made if possible. The error codes were recorded. Quo-Test was connected to a printer during the evaluation. All results were registered electronically in a spread sheet.

Evaluation of user-friendliness
Stine Beenfeldt Weber evaluated the user friendliness immediately after the hospital evaluation was performed. She used the evaluation form with the four categories; manual, time factors, control possibilities and operation facilities.

4.5.3. *Evaluation procedure in primary health care*
None of the primary health care centres analyses HbA1c in capillary samples, but both are used to handle capillary samples when measuring other analytes.

Training
The supplier, Triolab, was responsible for training on Quo-Test at the two primary health care centres. Triolab trained at both centres on the 12th of January 2011. On the same day, Stine Beenfeldt Weber trained the staff in logistic procedures. When the evaluation began, the evaluators had to handle Quo-Test on their own without any supervision or correction from the manufacturer/supplier. Questions were addressed to SKUP.

Recruitment of patients
Patients, which were going to have a routine HbA1c measurement, agreed to participate and have two capillary HbA1c measurement performed. Participation was voluntarily and verbal consent was considered sufficient. Capillary samples were collected from at least 40 patients in each primary health care centre.

Handling of samples and measurements
The patients had two capillary samples taken in two skin penetrations, following procedures in attachment 2. The first blood drop was wiped off, and second blood drop was used for analysis on Quo-Test. The capillary samples were measured immediately.
The samples from each patient were measured on one instrument and with test cartridges from the same lot number. Two different lot numbers were used in each primary health care centre.
One venous sample (a Greiner 3 mL tube with K_3DTA) per patient was collected for measurements on the comparison method. This sample was sent to the Department of Clinical Biochemistry, Hillerød Hospital.

Analysing with the comparison method
All samples were analysed twice on two different comparison method instruments. The time from blood sampling to analysis was maximum 48 hours. If the sample was not analysed on the same day as collected, it was kept at +4 °C until analysis the next day.

Quality assurance, Quo-Test
To monitor the quality of measurements on Quo-Test, two control materials from Quotient was analysed. One control was a high level control, and one was a low level control. One control was analysed in duplicate every other day, so that one control was analysed day 1, the other day 2 and so on.

Recording of results
All results were registered and signed by the evaluator. If an instrument showed an error code while analysing a sample, a new measurement was made, if possible. The error codes were recorded. Data were recorded in a form produced by SKUP.

Evaluation of user-friendliness
The evaluators filled in the user friendliness questionnaire after completing the practical work with the evaluation. They used the evaluation form with the four categories; manual, time factors, control possibilities and operation facilities.

5. Statistical expressions and calculations

This chapter with standardised text deals with the statistical expressions and calculations used by SKUP. The descriptions in section 5.2 are valid for evaluations of quantitative methods with results on the ratio scale.

5.1. Statistical terms and expressions

The definitions in this section originate from the ISO/IEC Guide 99; International Vocabulary of Metrology [19].

5.1.1. *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 measured as *imprecision*. Precision is descriptive in general terms (good, intermediate, poor e.g.), whereas the 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. CV is usually reported in percent.

To be able to interpret an assessment of precision, the precision conditions must be defined.
Repeatability is the precision of consecutive measurements of the same component carried out under identical measuring conditions (within the measuring series).
Reproducibility is the precision of discontinuous measurements of the same component carried out under changing measuring conditions over time. The reproducibility includes the repeatability.

5.1.2. *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 inversely related to systematic measurement error. Trueness is measured as *bias*. Trueness is descriptive in general terms (good, intermediate, poor e.g.), whereas the bias is reported in the same unit as the analytical result or in percent.

5.1.3. *Accuracy*

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

Accuracy is not a quantity and cannot be expressed numerically. A measurement is said to be more accurate when it offers a smaller measurement error. Accuracy can be illustrated in a difference-plot. Accuracy is descriptive in general terms (good, intermediate, poor e.g.).

5.2. Statistical calculations

5.2.1. *Statistical outliers*
The criterion promoted by Burnett [20] is 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 set to 5%. The segregation of outliers is made with repeated truncations, and all results are checked. Where the results are classified according to different concentration levels, the outlier-testing is carried out at each level separately. Statistical outliers are excluded from the calculations. Possible outliers will be commented on under each table.

5.2.2. *Calculations of imprecision based on duplicate results*
The precision of the field method is assessed by use of paired measurements of genuine patient sample material. The results are divided into three concentration levels, and the estimate of imprecision is calculated for each level separately, using the formula below [21]:

$$CV = \sqrt{\frac{\sum (d/m)^2}{2n}}$$

d = difference between duplicate measurements
m = mean of the duplicate measurements
n = number of differences

This formula is preferred when the coefficient of variation is constant across the concentration intervals.

5.2.3. *Calculation of bias (trueness)*
The mean deviation (bias) at different concentration levels is calculated based on results achieved under optimal measuring conditions. A paired t-test is used with the mean values of the duplicate results of the comparison method and the mean values of the duplicate results of the field method. The mean difference is shown with a 95% confidence interval.

5.2.4. *Assessment of accuracy*
The agreement between Quo-test and the comparison method is illustrated in a difference-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 the field method and the mean value of the duplicate results on the comparison method. The number of results within the quality goal limits is counted and assessed.

6. Results and discussion

6.1. Number of samples

In the hospital evaluation, 102 individuals having blood drawn for a routine HbA1c measurement participated with capillary measurements on Quo-Test instrument. One individual had not venous samples analysed with Quo-Test. Of the 102 capillary samples, 99 were duplicate measurements results and three were single results because the second sample resulted in an error In the primary health care evaluation, one centre recruited 40 patients and the other recruited 44 patients for duplicate measurements; however four results were single results because the second sample resulted in an error. An additional sample was not analysed on the comparison method.
All the duplicate results from the comparison method in this evaluation originate from two comparison method instruments.

Table 6. Number of test used with Quo-Test in the evaluation

The evaluation in hospital and primary health care centres	**Number of tests used**	
Hospital		
Measurements on capillary whole blood samples	102 x 2 - 3 =	201
Measurements on venous whole blood samples	101 x 2 =	202
Measurements on control samples	24 x 6 =	144
Invalid tests		16
Primary care		
Measurements on capillary whole blood samples	80 -2 +88 - 3 =	163
Measurements on control samples	28 + 34 =	62
Invalid tests *		14
n total		***~ 802***

*Five of the tests were invalid due to wrong handling

6.1.1. *Missing results or failed measurements*

In the hospital evaluation, there were 16 failed measurements. 13 were due to problems with the reagent in the test cartridges (codes 102 and 103), two due to insufficient blood (code 104), and one due to visually very low blood content in the collector. The failed measurements were distributed with seven error codes on the capillary, six on the venous and three on the control measurements. One venous duplicate measurement on Quo-Test was not performed.

In the primary health care evaluation, there were 14 failed measurements. Four were due to measurements made with cold test cartridges. Triolab specified in their training, that test cartridges must reach room temperature before analysis. One high control measurement was excluded because it was analysed in the “low control mode” on Quo-Test.
Primary health care centre 1 had five failed measurements distributed with three due to problems with the reagent in the test cartridges (codes 102 and 103) and two due to insufficient blood (code 104). In primary health care 2 one sample was not measured on the comparison method. The centre had four measurement errors due to insufficient blood (code 104) on Quo-Test, all from the same evaluator. The error code 104 (too little or too much blood) can occur because of problems with the coating of the blood collector; however it can also originate from faulty handling of the test. In total 18 of the failed mesurements were due to technical errors of the system.

Fraction of technical errors was: 18 / 802 * 100% = 2,2%

Conclusion
Quo-Test had 2,2% technical errors and did not fulfil the quality goal of a maximum of 2,0% waste due to technical errors.

6.1.2. *Excluded results*

For the capillary samples one difference between duplicate measurement (8,3 and 6,1% (DCCT)) was identified as an outlier, and one difference between the first Quo-Test result (6,7% and 5,6% (DCCT)) and the comparison method result (5,7 and 5,7% (DCTT)). For the venous duplicates there was one outlier (9,1 and 8,0% (DCCT)). Additional two results with Quo-Test were outliers compared to the comparison method. The first Quo-Test measurements were 5,8% and 7,3% (DCCT), the comparison method gave the results (6,8 and 6,9% (DCCT)) and (6,2 and 6,3% (DCCT)), respectively. These duplicate results, where the first measurement is identified as an outlier, are not used for calculations in the evaluation. The results are indicated in the difference plots.
The number of missing and excluded results is also mentioned under the tables and figures.

6.1.3. *Time schedule*

The evaluation period:

Hospital laboratory	9th of November 2010 to the 20th of February 2011
Primary health care centre 1	13th of January to the 3rd of May 2011
Primary health care centre 2	24th of January to the 29th of April 2011

6.2. Analytical quality of the selected comparison method

6.2.1. *The trueness of the comparison method*

Table 7. Bias of all Tosoh participants in the Labquality HbA1c EQA program 3044 in 2010-11

Survey	Quality Assurance Labquality HbA1c Sample	ERLTarget %(DCCT)	Tosoh group mean %(DCCT) n=23 to n=28	Bias %(DCCT) Tosoh-Target	Bias (%) (Tosoh-Target)/ Target x 100 n=23 to n=28
1/10	2	6,44	6,68	0,24	3,73
	1	4,96	5,11	0,15	3,02
2/10	2	9,25	9,53	0,28	3,03
	1	6,17	6,32	0,15	2,43
3/10	2	9,64	10,14	0,50	5,19
	1	6,32	6,53	0,21	3,32
4/10	2	9,90	10,35	0,45	4,55
	1	6,08	6,48	0,40	6,58
5/10	2	10,55	11,14	0,59	5,59
	1	6,29	6,39	0,10	1,59
1/11	2	8,19	8,60	0,41	5,01
	1	6,45	6,70	0,25	3,88
2/11	2	8,28	8,77	0,49	5,92
	1	6,12	6,40	0,28	4,58
Mean Tosoh group					**+4,17**

The Tosoh group has a bias of 4,17% compared to the European Reference Laboratory (ERL) for HbA1c in the Netherlands.

Discussion
Table 7 demonstrates the results of the Labquality HbA1c program 3044, where two fresh samples are distributed five times a year. The targets in the surveys originate from the European Reference Laboratory for Haemoglobin A1c, in the Netherlands, using two Secondary Reference Methods with different analytical principles: Menarini HA 8160 HPLC (ion exchange) and Primus HPLC (affinity).
In each survey the participant results are compared with the target value, with the all participants mean and with the peer group mean. 23 to 28 laboratories using Tosoh participated in the 2010-2011 survey. The average bias of the Tosoh participants was +4,17%. Thus the Danish quality goal for a comparison method, a bias less than ±3,0% was not fulfilled [5].

The Tosoh results from the Department of Clinical Biochemistry in Hillerød did not deviate from the Tosoh group. Triolab/Quotient wanted this evaluation to be performed according to the reference laboratory, with the HbA1c results adjusted for the bias of the Tosoh group.

Attachment 3 demonstrate that the deviation of the comparison method compared to the Tosoh group is -0,10%. The goal for the Department of Clinical Biochemistry with a bias less than 1,3% compared to the peer group mean was therefore fulfilled. The bias was checked in the range 5,11 to 11,14% (DCCT).

Adjustment of results
All results of the comparison method in this report are adjusted for the bias (+4,17%) of the Tosoh group compared to the European Reference Laboratory Target (table 7).

6.2.2. *Internal quality control with the comparison method*

Three internal control samples, one from DEKS and two fro Bio-Rad were analysed daily on the comparison method instruments. The results are shown in attachment 4.

For the DEKS control, that was analysed twice a day, the CV% for the three Tosohs (attachment 4) was less than 1% at the concentration 8,11% (DCCT) and the deviation was less than 0,6% for Tosoh 1 and Tosoh 3 used in the evaluation.

The Bio-Rad control was analysed once daily in two levels. The imprecision was less than 1,0 CV% for all Tosohs every month, except the Tosoh 1 in December 2009 and February 2010. Tosoh 1 had the column exchanged in February.

The differences between the Tosoh instruments in the laboratory have never been ≥0,4% (DCCT).

6.2.3. *The precision of the comparison method*

Table 8. Repeatability of the comparison method with venous whole blood EDTA patient samples

Level	Comparison method interval % (DCCT)	n	Excluded results	Tosoh G7 HbA1c mean % (DCCT)	*CV% (95% CI)
Low	4,6 — 5,6	34	0	5,2	0,9 (0,7 — 1,1)
Medium	5,6 — 6,8	34	0	6,1	0,8 (0,6 — 1,0)
High	6,9 — 11,9	34	0	8,2	0,8 (0,6 — 1,0)
All	4,6 — 11,9	102	0	6,5	0,8 (0,7 — 0,9)

*The calculated CV values are measures of imprecision under intermediate conditions. The duplicate measurements were often analysed within two days from sampling, and the duplicate results always originate from two different Tosoh G7 instruments.

6.3. Analytical quality of Quo-Test used in a hospital laboratory

6.3.1. *External quality assessment*

It is possible run EQA samples with the Quo-Test system.

6.3.2. *Internal quality control*

During the hospital evaluation one of the DEKS controls used daily on the comparison method instruments were also used on Quo-Test twice a day. The control materials from Quotient were analysed twice a day as well.

The reproducibility was assessed with the DEKS control and Quo-Test controls high and low using three lot numbers of tests. Control material may have other matrix effects than whole blood, and may therefore give other results than results achieved with blood. The reproducibility of Quo-Test is shown in table 9 and raw data are shown in attachment 5.

Table 9. Reproducibility of Quo-Test with control materials in the hospital laboratory

Material	n	mean HbA1c % (DCCT)	Reproducibility CV%
DEKS control	47	8,8	2,2
Quo-Test ”low”	48	6,7	3,6
Quo-Test ”high”	48	13,2	2,8

Discussion
The CV achieved with the control materials was 2,2%, 3,6% and 2,8% for the DEKS control, the Quo-Test “low” and “high” control material, respectively. The quality goal for imprecision, a CV less than 4,0% was achieved with the three control materials. These results show that the Quo-Test Quality Control is useful to check reproducibility for the Quo-Test, as is control material from DEKS.

6.3.3. *Comparison of the 1st and 2nd measurements*

Two capillary and two venous whole blood samples were taken from 99 and 101 individuals, respectively for measurements on Quo-Test. The assumption for using the formula in 5.2 is that there is no difference between the first and the second measurement. There was no systematic difference between the paired measurements (data not shown).

6.3.4. *The precision of Quo-Test*

Repeatability under standardised and optimal measuring conditions in a hospital laboratory was obtained with capillary (table 10) and venous whole blood samples (table 11).The raw data are not shown. Repeatability was calculated for three subgroups: the highest HbA1c-values (n=34), the lowest (n=34) and the middle level of HbA1c (n=34). The three groups are chosen according to their concentration with the comparison method.

Table 10. Repeatability of Quo-Test with capillary patient samples in the hospital laboratory

Level	Comparison method interval % (DCCT)	n	Excluded results	Quo-Test HbA1c mean % (DCCT)	CV% (95% CI)
Low	4,6 — 5,6	34	1*	5,0	5,2 (4,2 — 6,8)
Medium	5,6 — 6,8	34	4**	5,9	4,6 (3,7 — 6,1)
High	6,9 — 11,9	34	1***	8,2	2,0 (1,6 — 2,7)
All	4,6 — 11,9	102	6	6,4	4,2 (3,7 — 4,9)

The given numbers of results (n) are counted before the exclusion of outliers. Mean and CV are calculated after the exclusions. *One sample was a single measurement. ** two samples were single measurements, two results were outliers. *** one result was an outlier.

Table 11. Repeatability of Quo-Test with venous patient samples in the hospital laboratory

Level	Comparison method interval % (DCCT)	n	Excluded results	Quo-Test HbA1c mean % (DCCT)	CV% (95% CI)
Low	4,6 — 5,6	34	0	4,9	4,6 (3,8 — 6,1)
Medium	5,6 — 6,8	33	1*	5,9	3,3 (2,7 — 4,5)
High	6,9 — 11,9	34	1*	8,2	1,6 (1,3 — 2,2)
All	4,6 — 11,9	101	2	6,4	3,6 (3,2 — 4,3)

The given numbers of results (n) are counted before the exclusion of outliers. Mean and CV are calculated after the exclusions. *One result was an outlier.

Discussion

The calculated CV values are measures of repeatability. For the HbA1c % (DCCT) concentration intervals low, medium, and high the repeatability CV was 5,2%, 4,6%, and 2,0% with capillary samples and 4,6%,3,3%, and 1,6% with venous samples, respectively . The mean repeatability CV% for capillary samples results did not fulfill the quality goal (<4,0%) for samples with the concentrations above HbA1c below 6,8% (DCCT). For samples results above 6,8% (DCCT) the quality goal was fulfilled.

For the venous sample results the repeatability CV% was higher than the goal of 4,0% for the HbA1c concentrations below 5,6% (DCCT), while the goal was fulfilled for the concentrations above 5,6% (DCCT).

The CV% is significantly lower for the concentrations above 6,8% (DCCT) compared to the concentrations below 5,6% (DCCT) for both capillary and venous results.

The CV% achieved with genuine patient samples (table 10-11 and table 15) appear to be higher than the CV% for the control material (table 9). However, the concentration intervals are higher for the control materials. When comparing the CV% for results above 8,0% (DCCT) the CV% is 2,2% and 2,8% in control materials and 1,6% and 2,0% in genuine samples.

6.3.5. *The trueness of Quo-Test*

Bias (Quo-Test – (Tosoh, adjusted)/(Tosoh, adjusted) x 100) was calculated for the 102 patients divided in three subgroups of HbA1c values. The three groups were chosen according to their concentrations on the comparison method.

The distribution of the lots was: 36 patients were measured using lot 41, 33 patients were measured using lot 42 and 33 patients were measured using lot 46.

Table 12. Bias of Quo-Test HbA1c with capillary patient samples in the hospital laboratory

Level group	Comparison method Mean (interval) % (DCCT)	n	Excluded results	Bias % (DCCT) (95% CI)	Bias % (95% CI)
Low	5,2 (4,6 — 5,6)	34	1*	-0,2 ((-0,2) — (+0,1))	-3,1 ((-4,8) — (-1,4))
Medium	6,1 (5,6 — 6,8)	34	4**	-0,2 ((-0,2) — (-0,1))	-2,6 ((-3,9) — (-1,2))
High	8,2 (6,9 — 11,9)	34	1***	+0,1 ((+0,1) — (+0,2))	+0,6 ((-0,6) — (+1,7))
All	6,5 (4,6 — 11,9)	102	6	-0,1 ((-0,1) — (-0,0))	-1,6 ((-2,4) — (-0,7))

The given numbers of results (n) are counted before the exclusion of outliers. Mean and CV are calculated after the exclusions. *one sample was a single measurement. ** two samples were single measurements, two results were outliers. *** one result was an outlier.

Table 13. Bias of Quo-Test HbA1c with venous patient samples in hospital

Level group	Comparison method Mean (interval) % (DCCT)	n	Excluded results	Bias % (DCCT) (95% CI)	Bias % (95% CI)
Low	5,2 (4,6 — 5,6)	34	0	-0,2 ((-0,3) — (+0,2))	-4,6 ((−6,3) — (-2,9))
Medium	6,1 (5,6 — 6,8)	33	1*	-0,2 ((-0,3) — (-0,1))	-3,4 ((−4,4) — (-2,4))
High	8,2 (6,9 — 11,9)	34	1*	-0,0 ((-0,1) — (+0,1))	+0,1 ((−1,3) —(+1,4))
All	6,5 (4,6 — 11,9)	101	2	-0,1 ((-0,2) — (-0,1))	−2,7 ((−3,5) — (-1,9))

The given numbers of results (n) are counted before the exclusion of outliers. Mean and CV are calculated after the exclusions of outliers. *one result was an outlier.

Discussion

The quality goal, bias less than 4%, was fulfilled for capillary samples in all concentrations and for the venous samples with the concentrations of HbA1c above 5,6% (DCCT). Between 4,6 and 5,6% (DCCT) a bias of -4,6% was found for venous samples.

6.3.6. *The accuracy of Quo-Test*

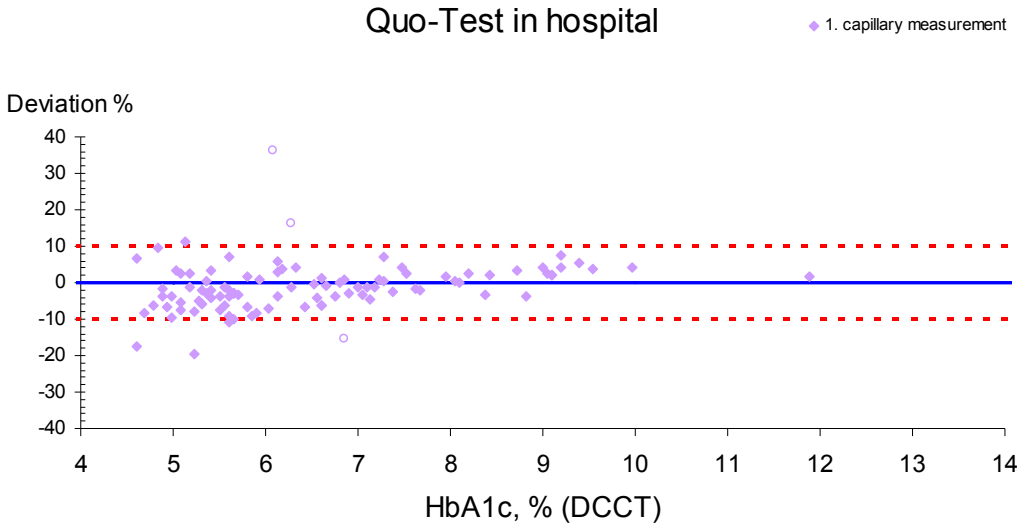

Figure 3. Difference plot showing the accuracy of the Quo-Test HbA1c results measured in capillary whole blood samples in the hospital laboratory. The x-axis represents the mean value of the duplicate results with the comparison method. The y-axis shows the deviation in percent between the first measurements on Quo-Test and the mean value of the duplicate results with the comparison method, n= 102. The open symbols represent the three outliers. Stippled lines represent allowable deviation ±10%.

Discussion and conclusion:
95% of the results should be within the allowable deviation to fulfil the quality goals for allowable deviation <±10%.
95 of 99 capillary sample results (96,0%) are within the maximal allowed deviation of ±10%.
In the hospital laboratory the capillary sample results fulfil the quality goals for accuracy.

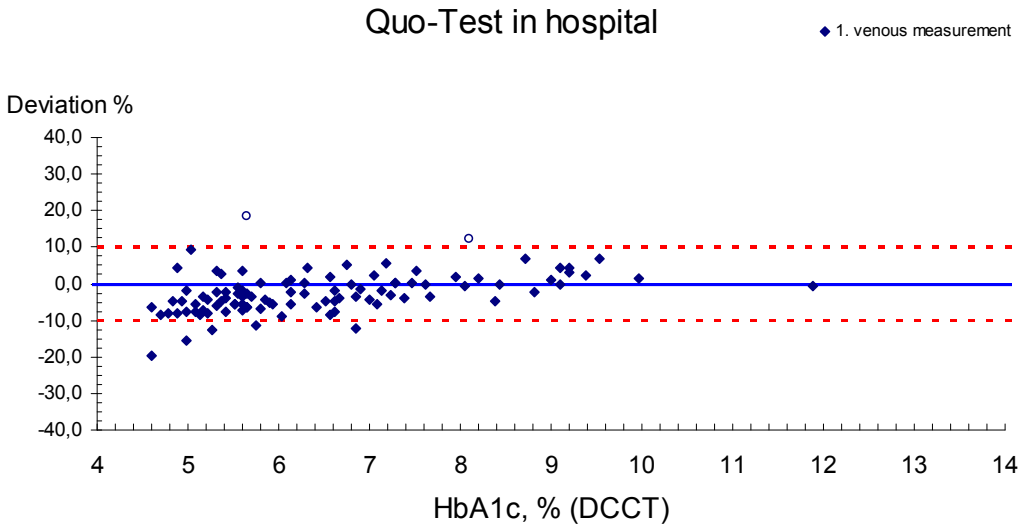

Figure 4. Difference plot showing the accuracy of the Quo-Test HbA1c results measured in venous whole blood samples in the hospital laboratory. The x-axis represents the mean value of the duplicate results with the comparison method. The y-axis shows the deviation in percent between the first measurements on Quo-Test and the mean value of the duplicate results with the comparison method, n = 101 including two outliers, open symbols. Stippled lines represent the allowable deviation ±10%

Discussion and conclusion:
95% of the results should be within the allowable deviation <±10% to fulfil the quality goal for accuracy.
Venous samples: 94 of 99 of the venous sample results (94,9%) are within the maximal allowed allowable deviation (±10%). The venous sample results in hospital laboratory do fulfil the quality goal for accuracy. It was noted that all results that deviated more than 10%, originated from lot 46, and most likely from the same card board case containing four boxes of tests.

6.4. Analytical quality of Quo-Test in primary health care

6.4.1. *Internal quality control*

The recommended internal quality control material was measured daily in both primary health care centres.

Table 14. Reproducibility of Quo-Test with the Quo-Test control material at the primary health care centres

Primary health care centre	Quo-Test control material	**N**	**mean HbA1c % DCCT**	**Reproducibility CV%**
1	low	14	6,9	5,2
	high	14	13,6	3,1
2	low	20	6,9	4,9
	high	16	12,9	2,8

Discussion:
The reproducibility CV with the recommended control material was 5,2 and 4,9% for the "low" control in primary health care – a little higher than in the hospital laboratory where the CV% with the same control material was 3,6%. For the "high" control, the CV% was 2,8 and 3,1% which is close to the CV% for the high genuine samples. It is also lower than the goal of <4,0 CV%.

6.4.2. *The precision of Quo-Test in primary health care centres*

The duplicate measurements on Quo-Test in primary health care were done with capillary samples. The results for the two centres are seen below. The evaluation was performed within four months in primary health care centre 1 and within three months in primary health care centre 2.

Table 15. Repeatability of Quo-Test on capillary samples in primary health care centre 1 and 2

Level	Comparison method interval % (DCCT)	n	Excluded results	Quo-Test HbA1c mean % (DCCT)	CV% (95% CI)
Primary health care centre 1					
Low	5,0 — 6,1	20	2*	5,5	5,1 (3,9 — 7,6)
High	6,1 — 10,4	20	0	6,9	3,4 (2,6 — 4,9)
All	5,0 — 10,4	40	2*	6,0	4,3 (3,5 — 5,5)
Primary health care centre 2					
Low	4,7 — 5,6	22	1**	5,1	3,6 (2,8 — 5,2)
High	5,6 — 9,0	22	4***	5,8	3,3 (2,5 — 4,9)
All	4,7 — 9,0	44	5	5,4	3,4 (2,9 — 4,5)

The given numbers of results (n) are counted before the exclusion of outliers. Mean and CV are calculated after the exclusions. *two single results. **one outlier. ***three single results.

Discussion:
Primary health care centre 2 did fulfil the quality goal of <4,0 CV% for both high and low HbA1c levels. Primary health care centre 1 did fulfilled the goal for HbA1c levels between 6,1 and 10,4% (DCCT), but not for lower HbA1c levels.

6.4.3. *The trueness of Quo-Test*

Bias was calculated for the 83 patients divided in two subgroups of HbA1c values. The two groups were chosen according to their concentrations on the comparison method.

Table 16. Bias of Quo-Test HbA1c with capillary patient samples in primary health care centre 1

Level Group	Comparison method Mean (interval) % (DCCT)	n	Excluded results	Bias (Quo-Test – Comparison method)	
				% (DCCT) (95% CI)	% (95% CI)
Primary health care centre 1					
Low	5,5 (5,0 — 6,0)	20	2*	+0,1 ((-0,0) — (+0,2))	+2,1((−0,0) — (+4,2))
High	7,2 (6,1 — 10,4)	20	0	-0,0 ((-0,1) — (+0,1))	-0,5 ((−2,3)— (+1,4))
All	6,4 (5,0 — 10,4)	40	2	+0,1 ((-0,0) — (+0,1))	+0,8((−0,6) — (+2,2))

Table 16. Bias of Quo-Test HbA1c with capillary patient samples in primary health care centre 2

Level Group	Comparison method Mean (interval) % (DCCT)	n	Excluded results	Bias (Quo-Test – Comparison method) % (DCCT) (95% CI)	 % (95% CI)
Primary health care centre 2					
Low	5,3 (4,7 — 5,6)	21	2**	-0,2 ((-0,3) — (-0,0))	-3,9 ((−6,1) — (-1,8))
High	6,2 (5,7 — 9,0)	22	3***	-0,2 ((-0,2) — (-0,0))	-2,7 ((−4,6) — (-0,8))
All	5,7 (4,7 — 9,0)	43	5	-0,2 ((-0,3) — (-0,1))	-3,3 ((−4,7) — (-1,9))

The given numbers of results (n) are counted before the exclusion of outliers. Mean and bias are calculated after exclusion of outliers. * two single results. ** one outlier. *** three single results.

6.4.4. *Accuracy of Quo-Test in primary health care centres*

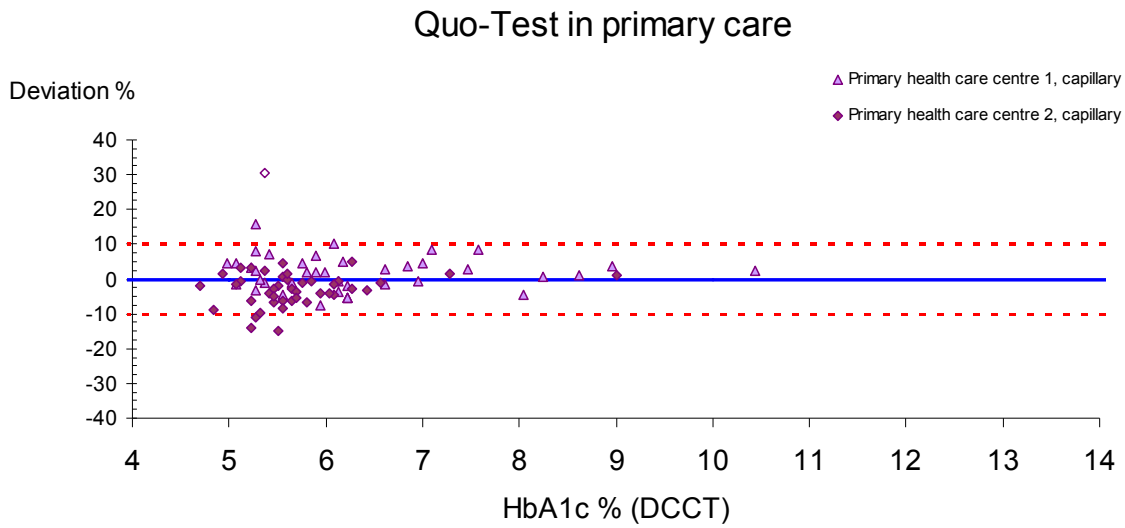

Figure 5. Difference plot showing the accuracy of the Quo-Test HbA1c results measured in capillary whole blood samples in two primary health care centres. The x-axis represents the mean value of the duplicate results with the comparison method. The y-axis shows the deviation in percent between the first measurements on Quo-Test and the mean value of the duplicate results with the comparison method, n = 83 including one outlier, open symbol. Stippled lines represent allowable deviation ±10%.

Discussion:

As seen in figure 5, four results deviated more than 10%, which means that 78 of 82 results (95,1%) fullfilld the accuracy goal. The primary health care centres therefore fulfilled the goal of an allowable deviation less than 10% for 95% of the samples.

6.5. The three lot numbers

Three lots of cartridges, 41, 42 and 46 were used in the evaluation. In the hospital evaluation for venous samples it was noted one outlier and the results that deviated more than 10% originated from lot 46. Therefore, the repeatability and bias in the hospital and the primary health centres were examined separately for the three lot numbers in use.

6.5.1. *The precision of lotnumbers on Quo-Test*

Table 17. Repeatability of Quo-Test with capillary patient samples with three lots of test cartridges in the two primary health care centres

Lot	Comparison method HbA1c interval % (DCCT)	n	Excluded results	Quo-Test HbA1c mean % (DCCT)	CV% (95% CI)
Primary health care centre 1					
42	5,0 — 9,0	18	1*	5,9	4,9 (3,8 — 7,3)
46	5,1 — 10,4	20	1*	6,0	3,6 (2,7 — 5,2)
Primary health care centre 2					
41	4,7 — 7,3	21	3**	5,4	3,6 (2,7 — 5,2)
46	4,8 — 9,0	23	2*	5,4	3,4 (2,6 — 4,9)

The given numbers of results (n) are counted before the exclusion of outliers. Mean and CV are calculated after the exclusions. * one result was a single result. ** one result was a single result, one was an outlier

Discussion

For repeatability, there were no differences between the three lots. In primary health care centres lot 41 and 46 fulfilled the quality goal for repeatability, less than 4,0 CV%. The CV% for lot 42 was 4,9% (CI 3,8-7,3%). In hospital laboratory, lot 41, 42 and 46 had CV% of 4,5%, 4,1% and 3,7% for the capillary samples, respectively, data not shown.

6.5.2. *The trueness of lot numbers on Quo-Test*

Table 18. Bias of Quo-Test HbA1c lot with capillary patient samples in hospital

	Comparison method Mean (interval) % (DCCT)	n	Excluded results	Bias % (DCCT) (95% CI)	Bias % (95% CI)
41	4,6 — 11,9	36	2*	-0,0 ((-0,1) — (+0,1))	-0,3 ((-1,5) — (+0,8))
42	4,9 — 9,2	33	1**	-0,1 ((-0,2) — (+0,0))	-1,7 ((-3,3) — (+0,0))
46	4,6 — 9,6	33	3***	-0,1 ((-0,2) — (-0,0))	-2,9 ((-4,4) — (-1,2))
All	4,6 — 11,9	102	6	-0,1 ((-0,1) — (+0,0))	-1,6 ((-2,4) — (-0,7))

The given numbers of results (n) are counted before the exclusion of outliers. Mean and CV are calculated after the exclusions. *one single measurement, one outlier. ** one outlier. *** two single measurements, one outlier.

Table 19. Lot dependent bias of Quo-Test HbA1c capillary samples in primary health care centres

Lot	Comparison method HbA1c interval % (DCCT)	n	Excluded results	Bias (Quo-Test – Comparison method)	
				% (DCCT) (95% CI)	% (95% CI)
Primary health care centre 1					
42	5,0 — 9,0	18	1*	+0,0 ((-0,1) — (+0,2))	+2,1((−0,0) — (+4,2))
46	5,1 — 10,4	20	1*	+0,1 ((-0,1) — (+0,2))	+0,9 ((−1,1)— (+3,0))
Primary health care centre 2					
41	4,7 — 7,3	21	3**	-0,2 ((-0,3) — (-0,0))	-2,8 ((−5,3) — (-0,4))
46	4,7 — 7,3	23	2***	-0,2 ((-0,3) — (-0,1))	-3,8 ((−5,3) — (-2,2))

The given numbers of results (n) are counted before the exclusion of outliers. Mean and bias are calculated after the exclusion of outliers. * one single result. ** one single result, one outlier and one was not measured on the comparison method. *** two single result.

Discussion

It is demonstrated that both hospital and the primary health care centres fulfil the goal of a bias <4,0% for all HbA1c concentrations and for the lot numbers used.

When combining the results from the hospital and primary health care centres it is seen that there is no significant differences between the different lots of test cartridges. In the hospital the results that deviated more than ±10% originated from the same case of test cartridges.

6.6. Evaluation of user-friendliness

6.6.1. *Questionnaire filled in by 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 the instrument. The questionnaire and the expressed opinions are presented in table 20 to 23. The first column shows what is up for consideration. The second column shows the rating by the individual users at the three evaluation sites. The third to fifth column show the rating options. Coloured frames mark the cells with the overall ratings from all evaluating sites. 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.

Unsatisfactory and intermediate ratings will be marked with an asterisk and explained below the table.

Table 20. Assessment of the information in the manual / insert

Information in manual / insert about:	Ratings (Color codes)	Overall rating: Red	Yellow	Green
General impression	G G G G Y	Unsatisfactory	Intermediate	Satisfactory
Table of contents	G – G G G	Unsatisfactory	Intermediate	Satisfactory
Preparations / Pre-analytic procedure	G – G Y G	Unsatisfactory	Intermediate	Satisfactory
Specimen collection	G G G Y Y	Unsatisfactory	Intermediate	Satisfactory
Measurement / Reading	G G Y G G	Unsatisfactory	Intermediate	Satisfactory
Measurement principle	Y G G G Y	Unsatisfactory	Intermediate	Satisfactory
Sources of error	G - - Y Y*	Unsatisfactory	Intermediate	Satisfactory
Fault-tracing / Troubleshooting	G - - Y G	Unsatisfactory	Intermediate	Satisfactory
Keyword index	G – G G G	Unsatisfactory	Intermediate	Satisfactory
Readability / Clarity of presentation	G – G G G	Unsatisfactory	Intermediate	Satisfactory
Available insert in Danish, Norwegian, Swedish	G – Y G G	Unsatisfactory	Intermediate	Satisfactory
Rating for the information in the manual				Satisfactory

* both of the evaluators at one primary health care centre evaluated this as intermediate because of wrong handling of some test cassettes (cassettes that were too cold were used). The evaluators were informed not to do this during training, and it is also specified in the manual.

There were no additional comments.

Table 21. Assessment of time factors

Time factors	Ratings (Color codes)	Red	Yellow	Green
Time for preparations / Pre-analytical time	G G G Y Y	>10 min	6 to 10 min.	<6 min.
Analytic time	G G G Y Y	>20 min	10 to 20 min.	<10 min.
Required training time	G G G G G	>8 hours	2 to 8 hours	<2 hours
Stability of test, unopened package	G – R R R*	<3 months	3 to 5 months	>5 months
Stability of test, opened package	Y R Y Y Y	<14 days	14 to30 days	>30 days
Rating of time factors				Satisfactory

***** When SKUP received the lots, there were more than six months until expiration, but when the primary care evaluation began, they were closer to expiration. Hence, the low rating from primary health care.

Positive comments: 'Easy to handle'
Negative comments: 'Very short stability on opened tests. This is not good'.

Table 22. Assessment of quality control possibilities

Quality control	Ratings (Color codes)	Red	Yellow	Green
Internal quality control	G - - - -	Un-Satisfactory	Intermediate	Satisfactory
External quality control	G - - - -	Un-Satisfactory	Intermediate	Satisfactory
Stability of quality control material, unopened	G – R - -	<3 months	3 to5 months	>5 months
Stability of quality control material, opened	G – Y - -	≤1 day	2 to 6 days	>6 days or disposable
Storage conditions for quality control materials, unopened	Y – Y - -	–20°C	+2 to +8°C	+15 to +30°C
Storage conditions for quality control materials, opened	Y – Y - -	–20°C	+2 to +8°C	+15 to +30°C
Usefulness of the quality control	G – R - -	Unsatisfactory	Intermediate	Satisfactory
Rating of quality control				Satisfactory

Positive comments:
Negative comments: 'Annoyingly short stability of control material'.

Table 23. Assessment of the operation facilities

Operation facilities	Ratings (Color codes)	Red	Yellow	Green
To prepare the test / instrument	G G Y Y G	Unsatisfactory	Intermediate	Satisfactory
To prepare the sample	G G Y Y G	Unsatisfactory	Intermediate	Satisfactory
Application of specimen	G G G G G	Unsatisfactory	Intermediate	Satisfactory
Specimen volume	G G G G G	Unsatisfactory	Intermediate	Satisfactory
Number of procedure step	G G Y G Y	Unsatisfactory	Intermediate	Satisfactory
Instrument / test design	G G Y G G	Unsatisfactory	Intermediate	Satisfactory
Reading of the test result	G G G G G	Difficult	Intermediate	Easy
Sources of errors	G - - Y G	Unsatisfactory	Intermediate	Satisfactory
Cleaning / Maintenance	G G – G G	Unsatisfactory	Intermediate	Satisfactory
Hygiene, when using the test	G G G G G	Unsatisfactory	Intermediate	Satisfactory
Storage conditions for tests, unopened package	Y - - - -	–20°C	+2 to +8°C	+15 to +30°C
Storage conditions for tests, opened package	G - - - -	–20°C	+2 to +8°C	+15 to +30°C
Environmental aspects: waste handling	Y Y Y G Y	Special precautions	Sorted waste	No precautions
Intended users	G G G G G	Biomedical scientists	Laboratory experienced	GP personnel or patients
Size and weight of package	G G G Y Y	Unsatisfactory	Intermediate	Satisfactory
Other comments about operation facilities (please specify)	- G Y - -	Unsatisfactory	Intermediate*	Satisfactory**
Rating of operation				Satisfactory

Positive comments:
- '**Nice with a response right away'
- 'If the quality of responses turns out good, then this is a fine instrument'
- 'Very easy to operate'

Negative comments:
- '*The waste takes up a lot of space'

6.6.2. *Assessment of the user-friendliness*

Five individuals evaluated the instrument and everyone were in general terms pleased with the instrument.

Some concerns were presented by the evaluators regarding the short stability of the reconstituted controls (seven days) and also the amount of waste generated by the system if you discard the test cartridges as sorted waste.

Overall, the instrument showed good user friendliness, and the evaluators expressed that Quo-Test was very easy to operate.

7. References

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Additional reading

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Attachments

1. Specifications and basic facts about the measurement system
2. Guide to sampling (in Danish)
3. Raw data, external control, comparison method
4. Raw data, internal control, comparison method
5. Raw data, internal control, the Quo-Test
6. Results, Quo-Test repeatability with three lots
7. Raw data HbA1C, Quo-Test results under standardised and optimal conditions
8. Raw data HbA1C, Quo-Test results from two primary health care centres
9. List of previous SKUP evaluations
10. Comments from the manufacturer

Attachment 1. Specifications and basic facts about the measurement system
Parts of this form are filled in by Triolab.

Table 1. Basic facts

Name of the measurement system:	Quo-Test™ A1c
Dimensions and weight:	Width: 205 mm Depth: 135 mm Height: 205 mm Weight: 1310 g
Available measurands with the evaluated system:	HbA1c
Measurand:	HbA1c
Sample material:	Capillary blood and EDTA stabilized whole blood
Sample volume:	4 µL
Measuring principle:	Boronate Fluorescence Quenching
Traceability:	IFCC European Reference Laboratory for Haemoglobin A1c, in the Netherlands
Calibration:	System calibrated for each reagent lot using data coded into a barcode provided with each box of cartridges – this barcode is read by the analyzer using the barcode scanner
Measuring range:	2 – 17% (DCCT)
Linearity:	not part of the evaluation
Measurement duration:	4 minutes
Operating conditions:	18 – 32 °C, 10-80% humidity
Electrical power supply:	100-240 VAC, 50-60 Hz, 30 W
Recommended regular maintenance:	Wiping with a damp cloth on the outside
Package contents:	One instrument, one barcode scanner, user manual
Necessary equipment not included in the package:	Finger prickers

Table 2. Post analytical traceability

Is input of patient identification possible?	Yes
Is input of operator identification possible?	Yes
Can the instrument be connected to a bar-code reader?	Yes, provided as standard
Can the instrument be connected to a printer?	Yes
What can be printed?	Date, time, result, lot number, instr. ID, test number, patient ID and operator ID is printed automatically after result appears on screen
Can the instrument be connected to a PC?	Yes
Can the instrument communicate with LIS (Laboratory Information System)? If yes, is the communication bidirectional?	Yes, via a Data Management System No
What is the storage capacity of the instrument and what is stored in the instrument?	7000 results
Is it possible to trace/search for measurement results?	Yes

Table 3. Facts about the test cartridges

Name of the reagent/test strips/test cartridges:	Quo-Test™ A1c Test Cartidges
Stability in unopened sealed vial:	Until expiration date (12 months from date of manufacture) at 2-8 °C, 1 month at room temperature
Stability in opened vial:	1 hour
Package contents:	Test Cartridge, Blood collector, , indicating desiccant (silica gel)

Table 4. Quality control

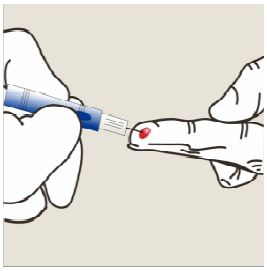
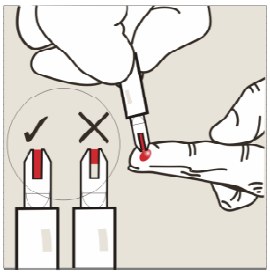
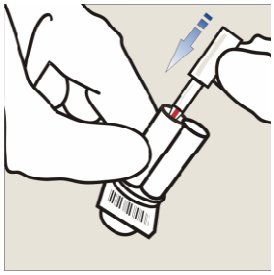
Electronic self check:	Yes
Recommended check materials and volume:	Quo-Test™ QC set (one high level and one low level)
Stability in unopened sealed vial:	Twelve months from production at +2 to +8 °C
Stability in opened vial:	14 days after reconstitution at +2 to +8 °C
Package contents:	2 controls (high and low), two pipettes, one bottle of water for reconstitution, control card, insert

Table 5. Marketing information

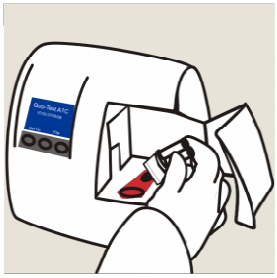
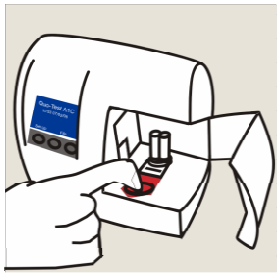
Manufacturer:	Quotient Diagnostics Ltd Unit 3 b, Russel House Molesey Rd Walton on Thames Surrey, KT12 3PE UK
Retailers in Scandinavia:	Denmark: Triolab AS Vallensbækvej 35 2605 Brøndby Phone: +45 4396 0012 Fax: +45 4396 4312 www.triolab.dk Norway: Medic 24 Hagebyvegen 40 3734 Skien Norway Phone: +47 35570300 Fax: +47 35570301 E-mail: info@medic24.no www.medic24.net Sweden: Medic24 AB Solvarvsgatan 4 SE-507 40 Borås Sweden Phone: + 46 33 23 00 99 Fax: + 46 33 23 00 28 E-mail: kundservice@medic24.se www.medic24.se
In which countries is the system marketed:	Globally X Scandinavia ☐ Europe ☐
Date for start of marketing the system in Scandinavia:	Pending SKUP (DK)
Date for CE-marking:	2/04/2009
In which Scandinavian languages is the manual available:	Danish, Norwegian and Swedish

Attachment 2. Guide to sampling (in Danish)

Udtagning af prøven

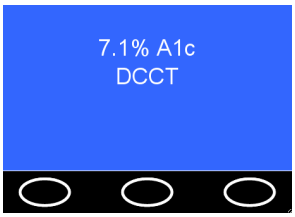
Trin 4 Brug en lancet til at prikke i patientens finger, så der kommer en god dråbe blod ud med ca. samme bredde som blodopsamleren.	
	**Trin 5** Sæt den spidse ende af blodopsamleren ind i bloddråben. Blodet skal fylde hele fordybningen i blodopsamleren.
Trin 6 Anbring blodopsamleren i hullet oven på kassetten. Sørg for, at blodopsamleren er kommet helt ind i kassetten og ikke stikker ud.	

Gennemførelse af testen

Trin 7 Åbn straks døren til analysatoren, og placer testkassetten i hullet bagerst i rummet. Sørg for, at kassetten siddet godt fast.	
	**Trin 8** Træk den røde tap ind mod dig. Testkasetten er nu fastlåst korrekt. Luk døren til analysatoren. Testen starter med det samme.
Trin 9 Når testen er afsluttet, vises resultatet på skærmen. Åbn døren, og skyd den røde tap væk fra dig. Tag kassetten ud, og bortskaf den på sikker vis. Luk døren.	

Testresultat

Når testen er afsluttet, vises resultatet på skærmen. Billedet nedenfor viser resultatet af en Quo-Test A1C-test som eksempel. I dette tilfælde var testresultatet 7,1% A1C. Bogstaverne "DCCT" under testresultatet viser, hvilken kalibreringsstandard der blev anvendt på det tidspunkt, testen blev udført. Det er vigtigt, da det fortæller dig og din læge, at Quo-Test A1C-resultatet kalibreres på samme måde som på hospitalernes klinisk biokemisk afdelinger.



Resultatet forbliver på skærmen, indtil du åbner døren til analysatoren og fjerner den brugte testkassette. Analysatoren er klar til endnu en test, så snart du har fjernet den brugte kassette.

Attachment 3: Raw data, external control, comparison method

Table 8. The comparison method, compared with the Tosoh group in Labquality HbA1c EQA pgr. 3044

Survey	Quality Assurance Labquality HbA1c program 3044, sample	Tosoh group mean n=23 to 28 % (DCCT)	Tosoh Hillerød % (DCCT)	No.	Hillerød-Tosoh group Δ HbA1c % (DCCT)	Δ HbA1c %
1/10	1	6,68	6,6	1	-0,08	-1,20
			6,6	2	-0,08	-1,20
			6,8	3	0,12	+1,80
	2	5,11	5,1	1	-0,01	-0,20
			5,1	2	-0,01	+0,20
			5,3	3	0,19	+3,72
2/10	1	9,53	9,5	1	-0,03	-0,31
			9,5	2	-0,03	-0,31
			9,5	3	-0,03	-0,31
	2	6,32	6,3	1	-0,02	-0,32
			6,3	2	-0,02	-0,32
			6,3	3	-0,02	-0,32
3/10	1	10,14	10,2	1	0,06	+0,59
			10,1	2	-0,04	-0,39
			10,1	3	-0,04	-0,39
	2	6,53	6,6	1	0,07	+1,07
			6,5	2	-0,03	-0,46
			6,5	3	-0,03	-0,46
4/10	1	10,35	10,2	1	-0,15	-1,45
			10,3	2	-0,05	-0,48
			10,2	3	-0,15	-1,45
	2	6,48	6,4	1	-0,08	-1,23
			6,5	2	0,02	+0,31
			6,4	3	-0,08	-1,23
5/10	1	11,14	11,0	1	-0,14	-1,26
			-	2	-	-
			10,9	3	-0,24	-2,15
	2	6,39	6,4	1	0,01	+0,16
			-	2	-	-
			6,3	3	-0,09	-1,41
1/11	1	8,6	8,6	1	0,00	0,00
			8,8	2	0,20	+2,33
			8,6	3	0,00	0,00
	2	6,7	6,7	1	0,00	0,00
			6,8	2	0,10	+1,49
			6,7	3	0,00	0,00
2/11	1	8,77	8,7	1	-0,07	-0,80
			8,9	2	0,13	+1,48
			8,7	3	-0,07	-0,80
	2	6,4	6,4	1	0,00	0,00
			6,5	2	0,10	+1,56
			6,4	3	0,00	0,00
mean					**-0,01**	**-0,10**

Attachment 4: Raw data, internal control, comparison method

Internal quality assurance (DEKS control) of the comparison method

DEKS control	2010					2011					
	August	September	October	November	December	January	February	March	April	May	all
Target (DCCT%)	8,11	8,11	8,11	8,11	8,11	8,11	8,11	8,11	8,11	8,11	
Mean Tosoh 1	8,2	8,2	8,2	8,2	8,3	8,1	8,1	8,2	8,1	8,0	8,16
Mean Tosoh 2	8,2	8,2	8,2	8,3	8,2	8,3	8,3	8,3	8,3	8,2	8,26
Mean Tosoh 3	8,1	8,1	8,1	8,2	8,1	8,1	8,2	8,2	8,2	8,2	8,15
n Tosoh 1	20	23	21	22	16	14	18	22	17	21	19,4
n Tosoh 2	21	23	15	21	19	22	19	22	16	20	19,8
n Tosoh 3	21	22	21	21	16	19	21	21	17	20	19,9
deviation Tosoh 1	0,1	0,1	0,1	0,1	0,2	0,0	0,0	0,1	0,0	-0,1	0,05
deviation Tosoh 2	0,1	0,1	0,1	0,2	0,1	0,2	0,2	0,2	0,2	0,1	0,15
deviation Tosoh 3	0,0	0,0	0,0	0,0	0,0	0,0	0,0	0,1	0,1	0,0	0,04
Bias% Tosoh 1	0,7	1,0	0,9	1,2	2,1	0,4	-0,2	0,6	0,0	-0,9	0,58
Bias% Tosoh 2	1,5	1,6	1,4	2,0	1,6	1,8	2,1	2,8	2,3	1,7	1,89
Bias% Tosoh 3	0,3	0,4	0,3	0,6	0,3	0,1	0,5	0,7	0,7	0,5	0,46
CV% Tosoh 1	0,6	0,5	0,7	0,9	1,7	0,6	2,5	0,6	0,4	0,7	0,92
CV% Tosoh 2	0,7	0,8	1,2	1,2	0,6	0,6	0,6	0,6	0,0	0,6	0,70
CV% Tosoh 3	0,6	0,7	0,7	0,6	0,7	0,7	0,9	0,6	0,6	0,6	0,68

Internal control sample results with the DEKS control 3 month before and during the evaluation period

Internal quality control result of HbA1c on the comparison method instruments before and during the evaluation

Biorad 1 control	2010					2011					
	August	September	October	November	December	January	February	March	April	May	all
Mean Tosoh 1	5,7	5,7	5,7	5,7	5,8	5,8	5,8	5,7	5,7	5,7	5,74
Mean Tosoh 2	5,8	5,8	5,8	5,8	5,8	5,9	5,9	5,9	5,9	5,9	5,85
Mean Tosoh 3	5,7	5,7	5,7	5,7	5,7	5,8	5,8	5,8	5,8	5,8	5,75
n Tosoh 1	38	43	37	43	30	31	38	43	32	40	37,5
n Tosoh 2	42	43	24	41	35	44	39	46	30	42	38,6
n Tosoh 3	42	39	36	43	31	36	40	44	31	39	38,1
CV% Tosoh 1	0,4	0,4	0,8	0,8	1,3	1,0	1,7	0,8	0,6	0,8	0,86
CV% Tosoh 2	0,8	0,7	0,8	0,9	0,5	0,6	0,4	0,6	0,4	0,5	0,64
CV% Tosoh 3	0,0	0,4	0,5	0,4	0,5	0,7	0,4	0,7	0,3	0,5	0,43

Biorad 2 control	2010					2011					
	August	September	October	November	December	January	February	March	April	May	all
Mean Tosoh 1	9,3	9,3	9,4	9,4	9,6	9,5	9,5	9,4	9,4	9,5	9,43
Mean Tosoh 2	9,4	9,4	9,4	9,4	9,4	9,5	9,6	9,6	9,6	9,6	9,49
Mean Tosoh 3	9,3	9,3	9,3	9,3	9,3	9,4	9,4	9,4	9,5	9,5	9,36
n Tosoh 1	39	40	37	43	28	30	39	43	32	40	37,1
n Tosoh 2	43	42	24	41	35	43	37	46	30	42	38,3
n Tosoh 3	42	39	37	43	30	36	40	44	31	39	38,1
CV% Tosoh 1	0,6	0,5	0,5	0,5	3,2	2,2	1,9	0,6	0,7	0,6	1,12
CV% Tosoh 2	0,7	0,8	1,0	1,0	0,6	1,0	0,5	0,5	0,5	0,4	0,70
CV% Tosoh 3	0,4	0,5	0,6	0,4	0,5	1,0	0,5	0,7	0,6	0,5	0,55

Internal control sample results three months before and during the evaluation period with the two Bio-Rad control materials.

Attachment 5. Raw data internal quality control, the Quo-Test

				Quo-Test					
Place	**Date**	**DEKS 1**	**DEKS 2**	**Low 1**	**Low 2**	**High 1**	**High 2**	**lot**	**Errors**
Hospital	09-11-2010	8,5	8,5	6,8	6,8	13,1	13,2	42	
Hospital	10-11-2010	8,9	-	6,6	6,8	13,0	12,9	46	
Hospital	11-11-2010	8,4	8,8	6,6	6,5	12,8	12,8	46	
Hospital	15-11-2010	8,8	8,8	6,3	6,4	12,6	12,6	41	
Hospital	22-11-2010	8,6	8,6	7,1	6,9	13,3	13,5	46	
Hospital	24-11-2010	9,2	8,8	6,7	6,6	13,2	13,1	42	
Hospital	25-11-2010	8,5	8,8	6,8	6,7	13,1	13,1	46	
Hospital	26-11-2010	9	8,9	6,5	6,3	12,9	12,7	41	
Hospital	29-11-2010	8,7	8,7	6,6	6,4	13,1	13,1	42	
Hospital	30-11-2010	8,8	8,9	6,9	7	13,6	13,4	42	QC-2: Error 102: out of range
Hospital	01-12-2010	8,8	9	6,8	6,8	13,5	13,5	42	
Hospital	02-12-2010	8,9	8,8	6,4	6,7	13,7	13,6	41	
Hospital	03-12-2010	8,9	8,6	6,9	6,8	13,4	14	41	
Hospital	06-12-2010	9,3	8,8	6,5	6,2	13	13,1	42	
Hospital	07-12-2010	8,6	9,2	6,9	6,6	13,4	12,8	46	
Hospital	14-12-2010	9	8,8	7,1	7	13,6	13,3	42	
Hospital	20-12-2010	8,6	8,9	6,6	6,5	13,3	13,8	46	DEKS-2: Error 103: out of range
Hospital	21-12-2010	8,9	9	6,4	6,4	13,1	12,8	42	
Hospital	17-01-2011	8,8	8,9	6,8	6,8	13,7	13,2	42	
Hospital	20-01-2011	8,9	8,7	6,7	6,5	12,7	13,2	46	
Hospital	22-02-2011	9	9,1	7,1	7	14,1	13,5	42	
Hospital	23-02-2011	8,9	8,6	6,8	6,6	12,9	12,9	46	
Hospital	24-02-2011	8,5	8,7	6,7	6,7	13,1	13,2	46	QC-1: Error 102: out of range
Hospital	25-02-2011	8,6	8,8	6,5	6,1	12,6	12,8	46	
Farum	14-01-2011					13,6	14,1	42	
Farum	17-01-2011			6,6	6,5			42	
Farum	18-01-2011			6,9	6,7	13,5	13,8	42	
Farum	19-01-2011			6,6	6,9			42	QC-2: Error 103: out of range
Farum	24-01-2011					13,7	13,7	42	
Farum	25-01-2011			7,1	6,8			42	
Farum	27-01-2011			6,4	6,8			42	QC-2: Error: result 10,4%
Farum	01-02-2011			7,2	7,7			42	
Farum	03-02-2011			6,9	6,8			46	QC-2: Error 102: out of range
Farum	08-02-2011					13,2	14,7	46	
Farum	22-02-2011					13,9	13,6	46	
Farum	24-02-2011					13,2	13,4	46	
Farum	02-03-2011					13,9	13,3	46	
Farum	03-03-2011			7,3	6,9			46	
Farum	07-03-2011			6,8	6,8			46	
Farum	25-03-2011			7,8	7,1			46	
Farum	30-03-2011					13,2	13	46	
Birkerød	24-01-2011					13,5	13	46	
Birkerød	26-01-2011			6,5	6,6			41	
Birkerød	02-02-2011					13,1	13,4	41	
Birkerød	04-02-2011			7	6,4			41	
Birkerød	07-02-2011					12,7	12,8	41/46	
Birkerød	08-02-2011			6,5	7			46	
Birkerød	09-02-2011					13,3	13	46	
Birkerød	02-03-2011			7,1	7,5			41	QC-2: Error 104: error reagent
Birkerød	09-03-2011					12,6	12,9	41	
Birkerød	06-04-2011			6,8	6,8			41	
Birkerød	11-04-2011					12,8	12,7	46	
Birkerød	12-04-2011			7,3	7,3			46	
Birkerød	28-04-2011					12,5	12,2	41	
Birkerød	29-04-2011			7,1	6,7			41	

Attachment 6. Results, Quo-Test repeatability with three lots.

Table 1. Repeatability of Quo-Test with capillary patient samples with the three lots in the hospital laboratory

Lot	Comparison method interval % (DCCT)	n	Excluded results	Quo-Test HbA1c mean % (DCCT)	CV% (95% CI)
41	4,6 — 11,9	36	2*	7,0	4,5 (3,7 — 6,0)
42	4,9 — 9,2	33	1**	6,0	4,1 (3,3 — 5,4)
46	4,6 — 9,6	33	3***	6,2	3,7 (3,0 — 5,0)
All	4,6 — 11,9	102	6	6,4	4,2 (3,7 — 4,9)

The given numbers of results (n) are counted before the exclusion of outliers. *one sample was a single measurement and one was an outlier ** one result was an outlier *** two samples were single measurements and one result was an outlier. Mean and CV are calculated after the exclusions.

Table 2. Repeatability of Quo-Test with venous patient samples with the three lots in hospital laboratory

Lot	Comparison method interval % (DCCT)	n	Excluded results	Quo-Test HbA1c mean % (DCCT)	CV% (95% CI)
41	4,6 — 11,9	35	0	6,9	2,9 (2,4 — 3,8)
42	4,9 — 9,2	33	1*	5,9	3,6 (3,0 — 4,9)
46	4,6 — 9,6	33	1*	6,1	3,8 (3,1 — 5,1)
All	4,6 — 11,9	101	2	6,4	3,6 (3,2 — 4,3)

The given numbers of results (n) are counted before the exclusion of outliers. *one result was an outlier. Mean and CV are calculated after the exclusions.

Attachment 7 Raw data HbA1C, Quo-Test results under standardised and optimal conditions

Attachment 8 Raw data HbA1C, Quo-Test results from two primary health care centres

Attachment 9 List of previous SKUP evaluations

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

SKUP evaluations between 1999 and 2011

Evaluation no.	Component	Instrument/testkit	Producer
SKUP/2011/91	HbA1c	Quo-Test	Quotient Diagnostics Ltd
SKUP/201190	CRP	*i*-CHROMA	Boditech
SKUP/2010/89*	Glucose	FreeStyle Lite	Abbott Laboratories
SKUP/2010/88	HbA1c	*Confidential*	
		Confidential	
SKUP/2011/86	Glucose[1]	OneTouch Verio	LifeScan, Johnson & Johnson
		Confidential	
		Confidential	
SKUP/2010/83*	Glucose	*Confidential*	
SKUP/2010/82*	Glucose, protein, blood, leukocytes, nitrite	Medi-Test URYXXON Stick 10 urine test strip and URYXXON Relax urine analyser	Macherey-Nagel GmBH & Co. KG
SKUP/2010/81*	Glucose	mylife PURA	Bionime Corporation
SKUP/2010/80	PT (INR)	INRatio2	Alere Inc.
SKUP/2010/79*	Glucose, protein, blood, leukocytes, nitrite	CombiScreen 5SYS Plus urine test strip and CombiScan 100 urine analyser	Analyticon Biotechnologies AG
SKUP/2010/78	HbA1c	In2it	Bio-Rad
SKUP/2010/77*	CRP	*Confidential*	
SKUP/2009/76*	HbA1c	*Confidential*	
SKUP/2009/75	Glucose	Contour	Bayer HealthCare
SKUP/2009/74	Glucose[1]	Accu-Chec Mobile	Roche Diagnostics
SKUP/2010/73	Leukocytes	HemoCue WBC	HemoCue AB
SKUP/2008/72	Glucose[1]	*Confidential*	
SKUP/2009/71	Glucose[1]	GlucoMen LX	A. Menarini Diagnostics
SKUP/2011/70*	CRP	smartCRP system	Eurolyser Diagnostica GmbH
SKUP/2008/69*	Strep A	Diaquick Strep A test	Dialab GmbH
		Confidential	
SKUP/2010/67	Allergens	*Confidential*	
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 &
SKUP/2005/39	Glucose[1]	OneTouch Ultra	LifeScan, Johnson &
SKUP/2004/38*	Glucose	GlucoSure Plus	Apex Biotechnology
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	RapidVue u-hCG	Quidel Corporation
SKUP/2004/34*	u-hCG	QuickVue u-hCG	Quidel Corporation
SKUP/2004/33	PT (INR)	Hemochron Jr. Signature	ITC International
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 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 Scandinavian market any more

Attachment 10 Comments from the manufacturer

QUOTIENT DIAGNOSTICS LIMITED
An EKF Diagnostics Company

SKUP
Dr. Esther Jensen, Stine Beenfeldt Weber MSc
Hillerød Hospital
Klinisk Biokemisk Afdeling
Dyrehavevej 29, indgang 16A
DK-3400 Hillerød
Denmark

Re: SKUP/2011/91, Quo-Test A1c: A system for the measurement of B-HaemoglobinA1c manufactured by Quotient Diagnostics Ltd.

We, in Quotient Diagnostics Limited (QDL), would like to express our gratitude to SKUP for the extensive evaluation of the Quo-Test A1c Test System. Our thanks are also extended to the operators who performed the analyses. We are very pleased that they rated the user-friendliness of the analyser as "satisfying" and that they found it very easy to operate.

The results obtained at both the hospital and at the two primary health care centres show that the Quo-Test may be used in a variety of settings. The performance of the Quo-test A1c in the hands of the SKUP evaluators is in line with the results achieved in the analysis of NGSP samples that resulted in the NGSP re-certification of QDL for the 2011/12 period. Furthermore, in the ongoing IFCC EQAS monitoring scheme we have achieved excellent correlation (r = 0.999) and a bias of 0.05% DCCT against the IFCC reference method.

Since the trial kits were shipped to SKUP approximately a year ago, there have been substantial improvements to our production procedures coupled with the introduction of an updated version of the Quo-Test software. This is attested by the good internal QC data obtained in the lots produced over the last 6 months where reagent errors have dropped significantly. We believe that these improvements would certainly reduce the number of technical errors obtained in the SKUP trial to less than the 2% limit.

We take the view that as the Quo-Test is primarily for monitoring the diabetic status of patients, where the accepted cut-off is currently 6.5% HbA1c, low imprecision around that value is very important.

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- In the critical range around the cut-off, 6% - 8% A1c, this SKUP study confirms that the test had an imprecision of 2.4% CV for capillary blood samples, and less than 2.0% CV for levels above 8% A1c.

The analysis of the results furthermore shows that Quo-Test A1c test performed consistently across three analysers and three different lots of reagents.

The comment regarding the short stability of the reconstituted controls has been addressed.

- At 2 - 8°C, shelf life stability of the controls is twelve months from date of manufacture and the reconstituted stability is 15 days. In addition, the control kit has been re-formatted with two vials of each of the high and low controls.

On-going real-time stability testing of the Quo-Test A1c cartridge has also resulted in the extension of its shelf-life from 9 to 12 months at 2 - 8°C.

QDL is continuously striving to improve these characteristics.

Overall, therefore, QDL is very pleased to have achieved such results in this rigorous and highly-regarded, independent evaluation. The SKUP trial has confirmed our view that the Quo-Test A1c is a suitable and reliable system for use in the monitoring of the diabetic status of patients in the primary care setting.

Yours Sincerely,

Brian E. Hickey
CEO, Quotient Diagnostics Ltd.

Walton-on-Thames, November 11, 2011