

Capitainer® B

A system for patient self-sampling of capillary blood for dried blood testing,
manufactured by Capitainer AB



Report from the evaluation

SKUP/2025/137

organised by SKUP at the request of Capitainer AB

www.skup.org

SKUP Scandinavian evaluation of laboratory equipment for point of care testing

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Attachments with raw data are included only in the copy to Capitainer AB.

1. Summary

Capitainer B, HbA1c

Manufacturer	Capitainer AB
Supplier in Denmark	You Do Bio
Supplier in Sweden	Same as the manufacturer
Supplier in Norway	Same as the manufacturer
Launched in Scandinavia	February 2020



Aim

To assess the analytical performance and user-friendliness of Hemoglobin A1c (HbA1c) measurements of capillary blood, collected with Capitainer B sampling card, analysed on Roche cobas pro with Tina-quant. Sample collection was performed by the intended users (health care personnel and lay persons), and measurements of HbA1c were performed by biomedical laboratory scientists. The first evaluation showed poor accuracy, therefore, a second evaluation was carried out after the manufacturer introduced changes to the pre-analytical procedure, as well as shortening the recommended stability time of the Capitainer B sampling card, from 14 to 5 days after sampling. The second evaluation included only Capitainer B samples collected by lay persons with diabetes, recruited at primary health care centers (PHCCs).

Performance specifications	Results	Conclusions
Repeatability CV $\leq 3,0$ %	First evaluation CV 1,4 – 2,8 %	Fulfilled when samples were collected by health care personnel.
	Second evaluation CV 0,8 – 1,3 %	Fulfilled when samples were collected by lay persons.
Accuracy ≥ 95 % of individual results within $\pm 3,0$ mmol/mol at HbA1c concentration $< 35,3$ mmol/mol and $\pm 8,5$ % at HbA1c concentration $\geq 35,3$ mmol/mol compared to the average result of the comparison method.	First evaluation 74,0 %	Not fulfilled when samples were collected by health care personnel.
	Second evaluation 89,0 %	Not fulfilled when samples were collected by lay persons.
User-friendliness A total rating of "Satisfactory"	First and second evaluation The user-friendliness was rated satisfactory.	Fulfilled

Additional information

Participants and evaluation sites	
<i>First evaluation</i>	113 persons with diabetes recruited at a hospital laboratory and 92 persons with diabetes recruited at three primary health care centres.
<i>Second evaluation</i>	115 persons with diabetes recruited at seven primary health care centres.
Evaluated method <i>Both evaluations</i>	HbA1c on capillary blood samples collected with Capitainer B sampling card, analysed on cobas pro c503 with Tina-quant.
Comparison method <i>Both evaluations</i>	cobas pro c503 with Tina-quant. HbA1c on venous whole blood samples.
Bias <i>Both evaluations</i>	When samples were collected by health care personnel in the first evaluation, a positive bias of 2,1 to 3,0 mmol/mol was observed between the evaluated method and the comparison method. When samples were collected by lay persons in the second evaluation, a positive bias of 0,7 to 2,1 mmol/mol was observed between the methods.

A letter with comments from Capitainer AB is attached to the report.

Further information about the evaluation and the organisation of SKUP can be found on www.skup.org. This summary is also published in Danish, Norwegian and Swedish at www.skup.org.

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2. Abbreviations and Acronyms

ACN	Application Code Number
APS	Analytical Performance Specification
BLS	Biomedical Laboratory Scientist
C-NPU	Committee on Nomenclature, Properties and Units
CI	Confidence Interval
CV	Coefficient of Variation
DEKS	Danish Institute of External Quality Assurance for Laboratories in the Health Sector
DSKB	The Danish Society of Clinical Chemistry
EDTA	Ethylenediaminetetraacetic acid
EQA	External Quality Assessment
Equalis	External quality assessment in laboratory medicine in Sweden
HbA1c	Haemoglobin A1c
IFCC	International Federation of Clinical Chemistry and Laboratory Medicine
Noklus	Norwegian Organization for Quality Improvement of Laboratory Examinations
NGSP	National Glycohaemoglobin Standardization Program
PHCC	Primary Health Care Centre
POC	Point of Care
SD	Standard Deviation
SKUP	Scandinavian evaluation of laboratory equipment for point of care testing
VUK	Videnskabeligt Udvalg for Kvalitetssikring (Scientific committee for quality assurance in Denmark)

3. Introduction

The purpose of Scandinavian evaluation of laboratory equipment for point of care testing (SKUP) is to improve the quality of near patient testing in Scandinavia by providing objective information about analytical performance and user-friendliness of laboratory equipment. This information is generated by organising SKUP evaluations in point of care (POC) settings.

3.1. The concept of SKUP evaluations

SKUP evaluations follow common guidelines and the results from various evaluations are comparable¹. The evaluation set-up and details are described in an evaluation protocol and agreed upon in advance. The analytical results and user-friendliness are assessed according to pre-set performance specifications. To fully demonstrate the performance of a product, the intended users should be involved in the evaluation. If possible, SKUP evaluations are carried out using three lot numbers of reagents from separate and time-spread productions. Some evaluation codes are followed by an asterisk (*), indicating an evaluation with a more specific objective. The asterisk is explained on the front page of these protocols and reports.

3.2. Background for the evaluations

Capitainer B is a microsampling card for the collection of a volumetrically defined dried blood sample, produced by Capitainer AB. The product is intended for use by health care personnel and lay persons. The sample material is fresh capillary whole blood. The capillary blood samples can be collected both in and outside of clinical settings with Capitainer B by the intended users and transported to a laboratory e.g. by regular mail, where measurement of numerous measurands is possible. For this evaluation, SKUP and the requesting company agreed to use haemoglobin A1c (HbA1c) as the measurand to assess the analytical performance of the capillary blood samples collected with Capitainer B for the purpose of analysing HbA1c. This decision was made because a verified method for measurement of HbA1c using Capitainer B is available, and SKUP has extensive experience in evaluating HbA1c. The Capitainer B sampling card was launched into the Scandinavian market February 2020. The SKUP evaluation was carried out during the summer and fall of 2024 at the request of Capitainer AB in Sweden.

After completion of the evaluation, the manufacturer introduced changes to the pre-analytical procedure of the method in response to initial poor accuracy. A second evaluation was thereby carried out during the spring and summer of 2025 at the request of Capitainer AB in Sweden (see section 7).

3.3. The aim of the evaluations

The aim of the evaluation was to assess the analytical performance of Capitainer B for the measurement of HbA1c, when performed in a hospital laboratory, and the user-friendliness of Capitainer B when used by the intended users, health care personnel and lay persons. The measurements of HbA1c were performed by biomedical laboratory scientists (BLSs) at a hospital laboratory.

¹SKUP evaluations are under continuous development. In some cases, it may be difficult to compare earlier protocols, results and reports with more recent ones.

3.4. The model for the evaluation of Capitainer B

SKUP evaluations for quantitative methods are based upon the fundamental guidelines in a book concerning evaluations of laboratory equipment in primary health care [1]. This evaluation consists of two parts (figure 1). One part of the first evaluation was carried out by health care personnel in a hospital laboratory. This part documents the performance of the Capitainer B under conditions as favourable as possible for achieving good analytical performance. The other part of the first evaluation was carried out by lay persons, recruited from primary health care centres (PHCCs). This part documents the performance of the Capitainer B when samples were collected outside of laboratory environment. In the second evaluation only the part with self-sampling by lay persons was performed. Both evaluations of Capitainer B included HbA1c measurements of reconstituted dried capillary blood samples, collected with Capitainer B sampling card and analysed on Roche cobas pro c 503 (Roche Diagnostics), with Tina-quant hemolysate application (application code number (ACN) 851), hereafter called “the Capitainer B/cobas pro system” (figure 2). The capillary blood samples collected with Capitainer B sampling card will hereafter be called “the Capitainer B samples”.

The evaluation included:

- Examination of the analytical performance (precision and accuracy) of the Capitainer B/cobas pro system when sampling was performed by health care personnel (first evaluation).
- Examination of the analytical performance (precision and accuracy) of the Capitainer B/cobas pro system when sampling was performed by lay persons (both evaluations).
- Evaluation of the user-friendliness of the sampling with Capitainer B and its manual/instructions by lay persons (first evaluation).
- Evaluation of the user-friendliness of the pre-analytical procedure for extraction and elution of Capitainer B and the instructions for this, by BLSs in a hospital laboratory (both evaluations).

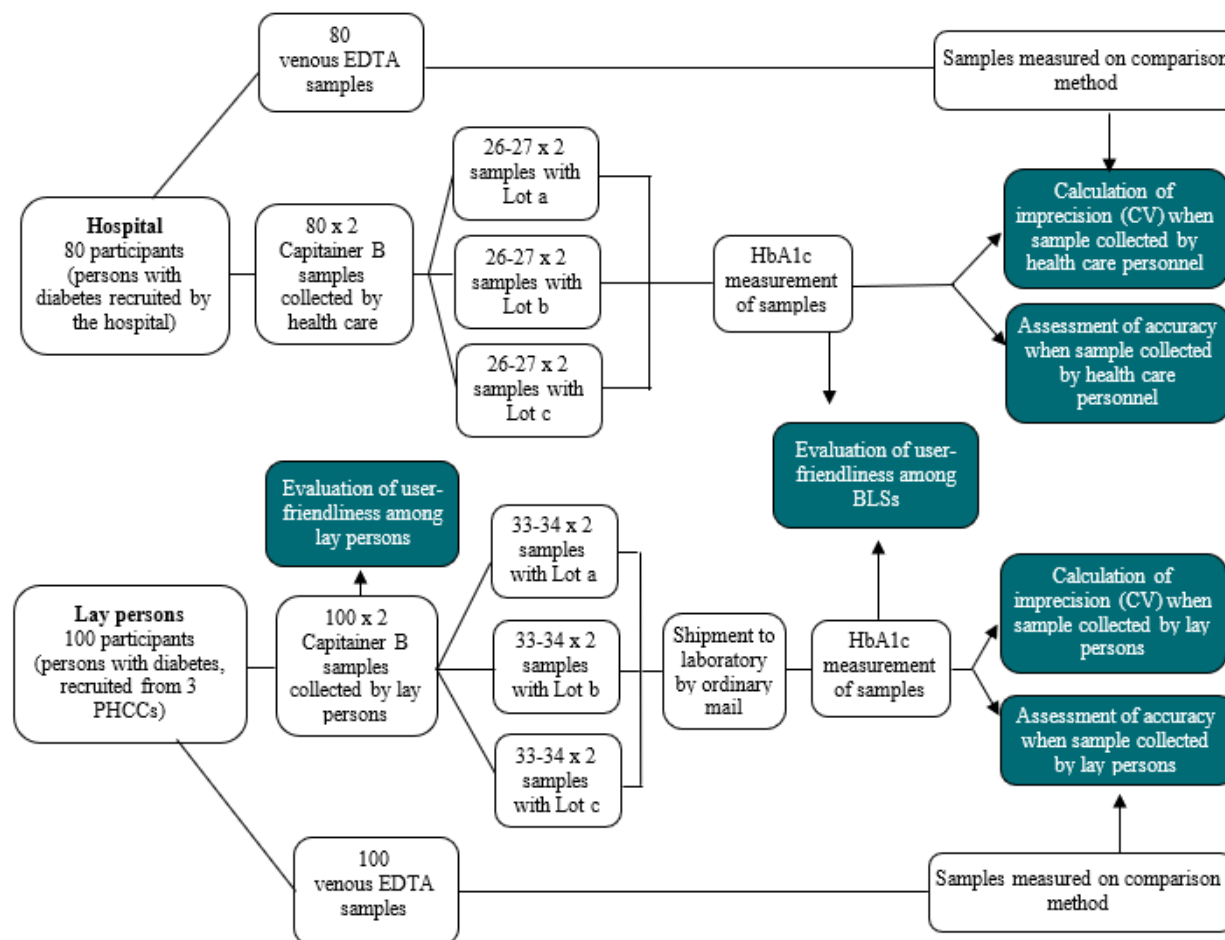
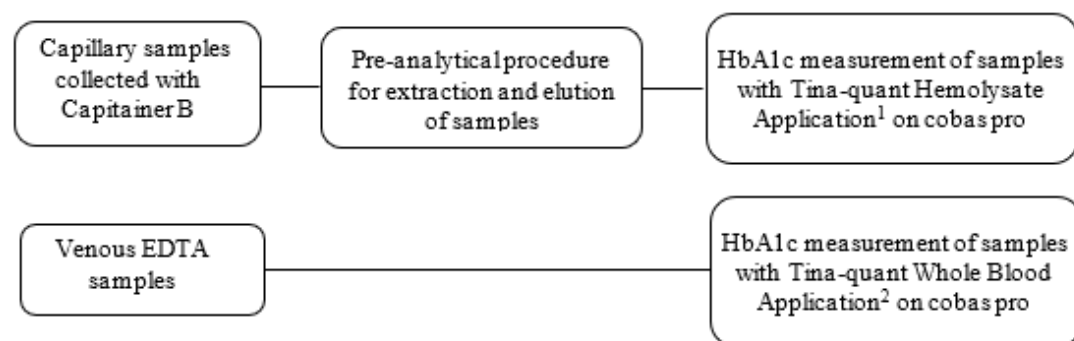


Figure 1: Flowchart illustrating the model for the evaluation of Capitainer B for the first evaluation. The second evaluation concerned only lay persons.



¹ACN 851

²ACN 881

Figure 2. The evaluation procedure for measurement of HbA1c in the hospital laboratory.

4. Performance specifications

4.1. Analytical performance specifications

The analytical performance specifications (APSs) in this evaluation are based on HbA1c results expressed in mmol/mol (IFCC units; International Federation of Clinical Chemistry and Laboratory Medicine). Performance specifications for HbA1c results in mmol/mol must be recalculated to performance specifications for results expressed in National Glycohaemoglobin Standardization Program (NGSP) units. Weycamp *et al.* [2] have explained why the APSs for HbA1c measurement in mmol/mol and Diabetes Control and Complications Trial (DCCT) % are different.

The Danish Society of Clinical Chemistry (DSKB) has a scientific committee for quality assurance Videnskabeligt Udvalg for Kvalitetssikring (VUK). In 2011, the committee specified the following performance specifications for HbA1c mmol/mol when used for diagnosis and monitoring of diabetes in Denmark [3]:

Maximum allowable imprecision coefficient of variation (CV): 2,8 %

Maximum allowable bias at HbA1c level 48 mmol/mol: $\pm 2,8$ %

Maximum allowable deviation at HbA1c level 48 mmol/mol: $\pm 7,3$ % (requirement for deviation from true target).

In 2021, VUK specified APSs for HbA1c mmol/mol for POC testing assessment by SKUP when used for diagnosis of diabetes [4]: The imprecision shall be ≤ 3 % and for the accuracy, at least 95 % of the individual HbA1c results shall fall within $\pm 3,0$ mmol/mol of the average measured values of the reference measurement procedure at HbA1c concentrations $< 35,3$ mmol/mol or within $\pm 8,5$ % at HbA1c concentrations $\geq 35,3$ mmol/L.

In Sweden, the national APSs are set up by external quality assessment in laboratory medicine in Sweden's (Equalis) advisory group for protein analysis and were approved by the Swedish Association for Clinical Chemistry in 2010 [5].

Maximum bias: $\pm 1,5$ mmol/mol

Between-laboratories-variation (CV): 2,5 %

Allowable deviation: bias + $1,65 \times$ standard deviation (SD) $\sim$ bias + $1,65 \times 0,025 \times$ HbA1c level

Thus, the allowable deviation at 48 mmol/mol is $\leq \pm 3,5$ mmol/mol.

The Norwegian Directorate of Health specified performance specifications for diagnostic use of HbA1c. The HbA1c method must be traceable to the IFCC reference method, and a deviation $\leq \pm 7,4$ % (in IFCC units) from reference target at a level of 48 mmol/mol and a CV < 3 % must be documented [6, 7].

Based on the national practices, SKUP chose to use a requirement of $\leq 3,0$ % for imprecision and to follow VUK for the APS of accuracy of HbA1c measurements. SKUP expected Capitainer B, when used for measurement of HbA1c, to have the same analytical performance as POC systems. Therefore, SKUP decided to use the same APSs for the evaluation of the Capitainer B/cobas pro system as for evaluation of POC systems for measurement of HbA1c. SKUP's performance specifications for HbA1c in this evaluation are as presented in section 4.3.

4.2. User-friendliness

The evaluation of user-friendliness was carried out by asking the evaluating persons to fill in a questionnaire, see section 6.6.

4.3. SKUP's performance specifications in this evaluation

As agreed upon when the protocol was drawn up, the results from the evaluation of Capitainer B are assessed against the following performance specifications:

Repeatability (CV)	$\leq 3,0 \%$
Allowable deviation of the individual result from the comparison method result for HbA1c concentrations $< 35,3$ mmol/mol	$\leq \pm 3,0$ mmol/mol
and for HbA1c concentrations $\geq 35,3$ mmol/mol	$\leq \pm 8,5 \%$
Required percentage of individual results within the allowable deviations.....	$\geq 95 \%$
User-friendliness, overall rating.....	Satisfactory

The results in this evaluation will only be presented in mmol/mol.

Results can be recalculated between the two units with the following equations:

$$\text{HbA1c (IFCC, mmol/mol)} = 10,93 \times \text{HbA1c (NGSP, \%)} - 23,54$$

$$\text{HbA1c (NGSP, \%)} = 0,0915 \times \text{HbA1c (IFCC, mmol/mol)} + 2,153$$

4.4. Principles for the assessments

For a system to be considered good in a SKUP evaluation, the system had to show satisfactory analytical performance as well as satisfactory user-friendliness.

4.4.1. Assessment of the analytical performance

The analytical results were assessed according to pre-set APSs.

Precision

The decision whether the achieved CV fulfils the APS or not, is made on a 5 % significance level (one-tailed test). The distinction between the ratings, and the assessment of precision according to the APS, are shown in table 1. Based on the results from each evaluation site, an overall conclusion was drawn in the summary of the report.

Table 1. The rating of precision.

Distinction between the ratings	Assessment according to the APS
The CV is equal to or lower than the APS (statistically significant)	The APS is fulfilled
The CV is equal to or lower than the APS (not statistically significant)	Most likely the APS is fulfilled
The CV is higher than the APS (not statistically significant)	Most likely the APS is not fulfilled
The CV is higher than the APS (statistically significant)	The APS is not fulfilled

Bias

SKUP did not set separate APSs for bias. The confidence interval (CI) of the measured bias was used for deciding if a difference between the evaluated method and the comparison method was statistically significant (two-tailed test, 5 % significance level). The bias was also discussed in connection with the accuracy.

Accordance between lot numbers

Separate lot-to-lot calculations were not performed. The results achieved with the three lots of sampling cards are visually shown in the assessment of accuracy in the difference plots for the results achieved by experienced laboratory personnel and the intended users. If there were distinct differences between the lots, these were pointed out and discussed.

Accuracy

The accuracy was illustrated in difference plots with limits for the allowable deviation according to the APS. The fraction of results within the limits was counted. The accuracy was assessed as either fulfilling the APS or not fulfilling the APS.

4.4.2. Assessment of the user-friendliness

The user-friendliness was assessed according to the answers and comments given in the questionnaire (see section 6.6 and 7.4.4). For each question, the evaluator could choose between three given ratings; satisfactory, intermediate and unsatisfactory, or the evaluator could mark the choice no opinion. The responses from the evaluators were reviewed and summed up. To achieve the overall rating “satisfactory”, the tested equipment had to reach a total rating of “satisfactory” in all three subareas of characteristics described in section 6.6 and 7.4.4

5. Materials and methods

5.1. Definition of the measurand

For Capitainer B, the sample material was fresh capillary whole blood, and for the comparison method the sample material was venous ethylenediaminetetraacetic acid (EDTA) blood. The results from HbA1c measurements are traceable to IFCC reference method and are expressed in the unit mmol/mol. The Committee on Nomenclature, Properties and Units (C-NPU) systematically describes clinical laboratory measurands in a database [8]. The NPU code related to the measurand in this evaluation is NPU27300. Some parts of the world only accept HbA1c results in NGSP unit (%), which is specified in NPU03835. In this report the term HbA1c was used for the measurand.

5.2. The evaluated sampling system Capitainer B

The information in this section derives from the company's information material.

Capitainer B (figure 3) is intended for use among health care personnel and lay persons.

The Capitainer B kit includes:

- Capitainer B sampling card
- Capitainer drying pouch

Capitainer B is a microsampling solution for the collection of a volumetrically defined dried blood sample.

The sampling card has two sample wells, each with a connecting control window. Each of the sample wells collect 10 µl capillary whole blood from a finger prick.

Capitainer B uses a combination of paper, polymer microfluids and thin water-soluble membranes to measure up a fixed volume of blood in each well.

When the blood is added to the inlet, a double valve solution is applied where a thin dissolvable membrane opens after blood application and excessive blood is removed at the inlet. Subsequently, a second membrane opens, allowing for transfer of the blood onto a sample collection disc. The system is developed to be easy to use and to have a guaranteed sample quality. A paper based drying pouch, that allows the sample to dry during transportation, is also included in the kit.



Figure 3. The Capitainer B sampling card.

When the blood is collected, the Capitainer B samples can be transported to a laboratory where the microsample is eluted before measurement. The sampling card can be used for the measurement of a variety of measurands. Capitainer AB offers three different solutions for the pre-analytical procedure of the Capitainer B samples; an automated, a semi-automated and a manual solution. The elution depends on the measurand and/or the instrument. For this evaluation a manual pre-analytical procedure developed at the Academic Laboratory at Uppsala University Hospital in Sweden, which includes haemolysing with a Tina-quant homolysing reagent, was used before measurement of HbA1c on cobas pro.

For more information about the Capitainer B sampling card, and name of the manufacturer and the suppliers in the Scandinavian countries, see attachment 1 and 2. For product specifications in the present evaluations, see attachment 3.

5.3. The selected comparison method

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

5.3.1. The selected comparison method in the evaluations

The selected comparison method in the evaluations was HbA1c measurements with Tina-quant on cobas pro c 503 (Roche Diagnostics) whole blood application, ACN 881, with venous EDTA samples, hereafter called “the comparison method”. The method is accredited according to SS-EN ISO15289 by the Swedish board for accreditation and conformity assessment (Swedac).

<i>Instrument:</i>	cobas pro, c 503
<i>Principle:</i>	Turbidimetric inhibition immunoassay (TINIA) for whole blood and hemolysate
<i>Traceability:</i>	Traceable to NGSP and IFCC [9,10]
<i>Calibrators:</i>	S1-S6: C.f.a.s. HbA1c
<i>Reagent:</i>	R1 Antibody reagent, R3 Polyhapten reagent and Hemolyzing reagent
<i>Reportable range:</i>	23 – 196 mmol/mol

Internal analytical quality control

Internal analytical quality control samples, two levels (PeciControl HbA1c norm and PeciControl HbA1c path, Roche Diagnostics) was measured each evaluation day on the comparison method.

External analytical quality control

The hospital laboratory participates in Equalis external quality assessment (EQA) scheme for HbA1c with one level in ten rounds per year (whole blood application on cobas pro). The assigned value for HbA1c is based on a consensus value of the five largest output groups.

5.3.2. Verification of the analytical performance of the comparison method

Precision

The repeatability (CV) of the comparison method was calculated from duplicate measurements of venous whole blood samples from the participants recruited at the hospital laboratory.

Trueness

The trueness of the comparison method was verified with EQA results for a period circumventing the evaluation period. No certified reference material was used to verify and adjust the method as both the Capitainer B samples and the comparison samples were measured with the same instrument using the same reagent.

5.4. The first evaluation

5.4.1. Planning of the evaluation

Inquiry about an evaluation

Capitainer AB via Mikael Ström, Business Development Manager, applied to SKUP in November 2022 for an evaluation of Capitainer B.

Protocol, arrangements and contract

In June 2024, the protocol for the evaluation was approved, and Capitainer AB and SKUP signed a contract for the evaluation. BLSs and assistant nurses, representing the intended users; health care personnel, at Laboratory medicine at Östersund Hospital, Sweden, were assigned to do the practical work with Capitainer B in the evaluation at the hospital laboratory. Three PHCCs in Östersund agreed to recruit participants for the evaluation; Krokoms hälsocentral, Odensala hälsocentral and Zätaagränds hälsocentral. The participants recruited at the PHCCs represented the intended users, lay persons.

Training

Capitainer AB was responsible for the necessary training for the pre-analytical procedure including extraction, elution and haemolysis for Capitainer B samples for measurement on the comparison method. The training was given in the local language and the training procedure reflected the training usually given to the end-users. When the evaluation had started, Capitainer AB was not allowed to contact or supervise the persons at the evaluation sites directly, all communication had to go through SKUP. Capitainer AB provided written instruction for sampling on the Capitainer B sampling cards. No actual training of the sampling on the Capitainer B sampling cards was provided.

5.4.2. Evaluation sites and persons involved

The practical work was carried out over 12 weeks at the hospital laboratory and 18 weeks in the PHCCs, ending in October 2024. At the hospital laboratory 18 BLSs were involved in the practical work with the evaluation of Capitainer B. All of them performed HbA1c measurements on routine venous samples using the comparison method. Only two of the BLSs performed the preanalytical procedure and HbA1c measurements of the Capitainer B samples. Three assistant nurses were involved in the sampling with Capitainer B at the hospital laboratory.

Three PHCCs participated in the evaluation. The health care personnel at the evaluation sites were responsible for the recruitment of participants and collecting the venous routine sample for the comparison method.

5.4.3. The evaluation procedure at the hospital laboratory

Recruitment of participants and ethical considerations

Persons with diabetes, 18 years or older, coming into the hospital laboratory for HbA1c measurements were asked if they were willing to donate two capillary samples for the evaluation, in addition to the routine venous samples. Persons with known haemoglobinopathies, haemolytic anaemia or pregnancy were not included. Privacy protection of the participants was secured; no personal information was collected, and no result from the evaluation can be traced to individual participants. Participation was voluntary and verbal informed consent was considered sufficient. Ethical approval was not necessary because the evaluation was considered a quality assurance project.

Handling of the samples and measurements

Fresh capillary blood samples were collected with Capitainer B. Three lot numbers of sampling cards were used, alternating between the lot numbers. The puncture site was disinfected with alcohol pads and allowed to dry completely before sampling. Disposable lancing devices, BD Microtainer Contact Activated Lancet Blue with depth settings 2,0 mm were used. The first drop was wiped off with a swab, and the second drop was collected with Capitainer B in accordance with the instructions from the manufacturer. The complete sampling was repeated for the second sample well of the same sampling card. Upon arrival at the laboratory, a pre-analytical procedure for the Capitainer B sample was performed, including extraction, elution and haemolysis of the sample, see attachment 5. The pre-analytical procedure and measurements with the Capitainer B/cobas pro system were preferably performed within 7 days and at latest within 14 days of sampling in agreement with the requesting company. The Capitainer B samples were stored at 15 – 28°C from arrival at the laboratory until preparation and measuring. The pre-analytical procedure and the measurements were performed on the same day.

The venous samples for the comparison method were obtained from one venous puncture and collected into a BD Vacutainer EDTA tube. The tubes were inverted 5 – 10 times to ensure thorough mixing. The venous samples were measured in duplicate on the comparison method within 72 hours of collection. All samples were treated according to the internal procedures of the hospital laboratory regarding potential interfering substances.

5.4.4. The evaluation procedure in primary health care

Recruitment of participants

Persons with diabetes, 18 years or older, coming into the PHCC for HbA1c measurements were asked if they were willing to self-sample two capillary whole blood samples and donate one venous blood sample for the evaluation. Persons with known haemoglobinopathies, haemolytic anaemia or pregnancy were not included. Privacy protection of the participants was secured; no personal information of the participants was obtained and no result in the evaluation can be traced to individual participants. Participation was voluntary and written informed consent was considered sufficient. Ethical approval was not necessary because the evaluation was considered a quality assurance project.

Handling of the samples and measurements

Fresh capillary blood samples were self-sampled by the participants using Capitainer B. The puncture site was disinfected with alcohol pads and allowed to dry completely before sampling. Disposable lancing devices, BD Microtainer Contact Activated Lancet Blue with depth settings 2,0 mm was used. The first drop was wiped off with a swab and the second drop was collected with Capitainer B in accordance with the instructions from the manufacturer. The complete sampling was repeated for the second sample well of the same sampling card. The sampling procedure was performed at the PHCC without guidance or help from the health care personnel. The sampling card was sent within 3 days by regular mail to the hospital laboratory. Upon arrival at the laboratory, a pre-analytical procedure for the Capitainer B sample was performed, including extraction, elution and haemolysis of sample, see attachment 5. The pre-analytical procedure and measurements with the Capitainer B/cobas pro system were preferably performed within 10 days and at latest within 30 days of sampling in agreement with the requesting company. The Capitainer B samples were stored at 15 – 28°C from arrival at the laboratory until preparation and measuring. The pre-analytical procedure and the measurements were performed

on the same day. As the sampling cards were sent by regular mail, the storage temperature may have deviated for short periods. This part of the evaluation mimicked the real-life conditions where lay persons are supposed to collect the samples themselves and then send the sampling card by mail to a hospital laboratory for analysis. Three lot numbers of Capitainer B were used at the PHCCs during the evaluation. Each of the PHCC used a single lot number throughout the entire period.

Samples for the comparison method were obtained from venous sampling and collected into a BD Vacutainer EDTA tube. The tubes were inverted 5 – 10 times to ensure thorough mixing. The venous samples were transported to the hospital laboratory and measured on the comparison method upon arrival. A duplicate measurement of the venous sample was performed if the Capitainer B sample arrived at the lab within 72 hours. The BLSs at the hospital laboratory were not able to identify which sample to be measured in duplicates before arrival of the corresponding Capitainer B sample. If the Capitainer B sample arrived after 72 hours, the venous sample had exceeded the validated stability time for the comparison method and was thus excluded. All samples were treated according to the internal procedures of the hospital laboratory regarding potential interfering substances.

6. Results and discussion, first evaluation

Statistical expressions and calculations used by SKUP are shown in attachment 4.

6.1. Number of samples

The scheduled number of samples in the first evaluation was 80 participant samples collected and measured in duplicate at the hospital laboratory and 100 participant samples collected in duplicate at the PHCCs and measured at the hospital laboratory.

At the hospital laboratory 113 participants were recruited (SKUP ID 1 – 113). From the PHCC's 92 participants were recruited (SKUP ID 1001 – 1092). The results from the comparison method covered the HbA1c interval 28 – 88 mmol/mol. The evaluation was carried out using three lot numbers of Capitainer B. The hospital laboratory was alternating between the lot numbers, while the three PHCC's used one lot number each. Due to a misunderstanding at the hospital laboratory, the lot numbers of the first 22 Capitainer B samples were not recorded. An account of the number of samples not included in the calculations, is given below.

Missing results

- ID 80; results are missing due to an error on the cobas pro system.
- ID 1002, 1048 and 1075; the measurement of Capitainer B samples collected by lay persons was missing due to incomplete sampling or no sample in the filter.
- Six Capitainer B samples collected by health care personnel and 15 Capitainer B samples collected by lay persons; one of each duplicate results were reported as missing (IDs, see attachment 6). The single measurements were included in the calculation of bias and the assessment of accuracy but not included in the calculation of Capitainer B repeatability.
- For the comparison method only single measurements were reported for 59 of the venous blood samples collected at the PHCCs (IDs, see attachment 6) as the venous samples had exceeded the validated stability time for the comparison method before the second measurement (see section 5.4.3). The single measurements were included in the calculation of bias and the assessment of accuracy but not included in the calculation of the comparison method repeatability.

Omitted results

There were no omitted results.

Excluded results (statistical outliers)

Statistical outliers in SKUP evaluations are detected by the criterion promoted by Burnett [11]. Statistical outliers:

- ID 43 and ID 82; the results from the Capitainer B samples were classified as outliers according to Burnett's model in the calculation of repeatability and therefore not included in the calculation of repeatability and bias of Capitainer B but were included in the assessment of accuracy (the first of the duplicate measurements).
- ID 113; the results from the comparison method were classified as outliers according to Burnett's model in the calculation of repeatability and therefore not included in the calculation of repeatability for the comparison method, bias and accuracy.
- ID 1025; the results from the Capitainer B samples were classified as outliers according to Burnett's model in the calculation of bias and therefore not included in the calculation of bias,

but the results were included in the calculation of repeatability and accuracy (the first of the duplicate measurements).

6.2. Analytical performance of the selected comparison method

6.2.1. Internal analytical quality control

All results from the internal analytical quality controls (PreciControl HbA1c Norm and Path), two levels, were within the allowable control limits (data not shown). The internal analytical quality controls were measured on Roche cobas pro c 503 with Tina-quant whole blood application (ACN 881).

6.2.2. The precision of the comparison method

Duplicate measurements of each venous whole blood sample were performed on the comparison method. The results were checked visually to meet the imposed condition for using formula 1 in attachment 4. There were no systematic differences pointed out between the paired measurements (data not shown).

The precision is presented as repeatability (CV). The CV with a 90 % CI is shown in table 3. The results were sorted and divided into three concentration levels according to the mean of the results. Raw data is attached for the requesting company only, see attachment 6.

Table 2. Repeatability (CV) of the comparison method for HbA1c measured in venous whole blood samples.

Level	n*	Excluded results (statistical outliers)	Mean value HbA1c, mmol/mol	CV (90 % CI), %
1	47	0	35,5	1,4 (1,2 – 1,7)
2	52	1**	45,4	0,8 (0,7 – 0,9)
3	13	0	67,6	0,9 (0,7 – 1,3)

*The given number of results (n) were counted before the exclusion of statistical outliers. Mean and CV were calculated after the exclusion of statistical outliers. An account of the number of samples is given in section 6.1.

**ID 113 was a statistical outlier according to Burnett's model [11] in the calculation of repeatability and therefore excluded.

Discussion

The CV for the comparison method was between 0,8 and 1,4 %.

6.2.3. The trueness of the comparison method

The trueness of the comparison method was verified with EQA results. The results from two HbA1c EQA surveys from Equalis (specified in section 5.3.1) are shown in table 4.

Table 4. EQA control material from Equalis measured on the comparison method.

Period of survey	Assigned value, HbA1c mmol/mol (acceptance limits)	n	Result cobas pro c 503, HbA1c mmol/mol
2024:06	39,8 ± 3,14 (35,76 – 42,94)	1	40,7
2024:07	45,1 ± 3,36 (41,74 – 48,46)	1	46,6

Discussion

The trueness of the comparison method was confirmed by the results in the national EQA scheme for HbA1c.

6.3. Analytical performance of Capitainer B/cobas pro system when samples collected by health care personnel

The results below reflect the analytical performance of Capitainer B when the samples were collected by health care personnel at the hospital laboratory and analysed by BLSs at the hospital laboratory.

All results from the internal analytical quality controls (PeciControl HbA1c Norm and Path), two levels, were within the allowable control limits (data not shown). The internal analytical quality controls were measured on Roche cobas pro c 503 with Tina-quant hemolysate application (ACN 851).

All Capitainer B samples collected by health care personnel were measured within 4 days of collection with an average time of 2 days (data not shown).

6.3.1. The precision of Capitainer B/cobas pro system

Two measurements of the capillary whole blood sample, one from each of the sample discs of the Capitainer B, were performed. Meaning that two separate elutions were performed, one for each sample disc, so that the two measurements come from different blood drops, and separate elution wells. The results were checked visually to meet the imposed condition for using formula 1 in attachment 4. There were no systematic differences pointed out between the paired measurements (data not shown).

The precision is presented as repeatability (CV). The CV with a 90 % CI is shown in table 5. The results were sorted and divided into three concentration levels according to the mean of the results of the Capitainer B samples. Raw data is attached for the requesting company only, see attachment 7.

Table 5. Repeatability (CV) of Capitainer B samples measured for HbA1c. Results achieved when the samples were collected by health care personnel.

Level	n*	Excluded results (statistical outliers)	Mean value HbA1c, mmol/mol	CV (90 % CI), %
1	24	1**	35,6	2,8 (2,3 – 3,8)
2	66	0	45,1	2,5 (2,2 – 2,9)
3	16	1**	67,6	1,4 (1,0 – 2,0)

*The given number of results (n) were counted before the exclusion of statistical outliers. Mean and CV were calculated after the exclusion of statistical outliers. An account of the number of samples is given in section 6.1.

**ID 43 and ID 82 were statistical outliers according to Burnett's model [11] in the calculation of repeatability and therefore excluded.

Discussion

The CV achieved by health care personnel at the hospital laboratory was between 1,4 and 2,8 % depending on the concentration level. The CV was statistically significantly lower than the APS for level 2 and 3. However, the CV was not statistically significantly lower than the APS for level 1, since the upper limit of the CI exceeded the APS of $CV \leq 3,0$ %.

Conclusion

When Capitainer B samples was collected by health care personnel and measurements on cobas pro was performed by BLSs the APS for repeatability ($CV \leq 3,0$ %) was fulfilled in level 2 and 3 and most likely fulfilled in level 1.

6.3.2. The bias of Capitainer B/cobas pro system

The mean deviation (bias) of Capitainer B sample results from the comparison method was calculated. The bias is presented with a 95 % CI in table 6. The results were sorted and divided into three concentration levels according to the mean results of the comparison method. Raw data is attached for the requesting company only, see attachments 6 and 7.

Table 6. Bias of Capitainer B samples measured for HbA1c. Results achieved when the samples were collected by health care personnel.

Level	n	Excluded results (statistical outliers)	Mean value Comparison method, HbA1c, mmol/mol	Mean value Capitainer B, HbA1c, mmol/mol	Bias (95 % CI), mmol/mol	Bias, %
1	46	0	35,6	37,9	2,2 (1,9 – 2,6)	6,3
2	51	0	45,4	48,4	3,0 (2,6 – 3,5)	6,6
3	12	0	67,2	69,2	2,1 (1,4 – 2,8)	3,1

An account of the number of samples is given in section 6.1.

Discussion

There was a statistically significant bias between the results from the Capitainer B samples and the comparison method in all concentration levels. The results from the Capitainer B samples were systematically higher than the results from the comparison method, ranging from 2,1 to 3,0 mmol/mol.

6.3.3. The accuracy of Capitainer B/cobas pro system

To evaluate the accuracy of the HbA1c results from the Capitainer B samples, the agreement between Capitainer B samples and the venous samples analysed on the comparison method is illustrated in a difference plot (figure 4). The limits for the allowable deviation according to the APS, within $\pm 3,0$ mmol/mol of the results of the comparison method for HbA1c concentrations $< 35,3$ mmol/mol and within $\pm 8,5$ % for HbA1c concentrations $\geq 35,3$ mmol/mol, are shown with stippled lines. The plot includes the deviation in HbA1c concentration between the first measurement of each Capitainer B sample against the mean result of the corresponding sample of the comparison method. The plot illustrates both random and systematic errors, reflecting the total measuring error in the results from the Capitainer samples. Raw data is attached for the requesting company only, see attachments 6 and 7.

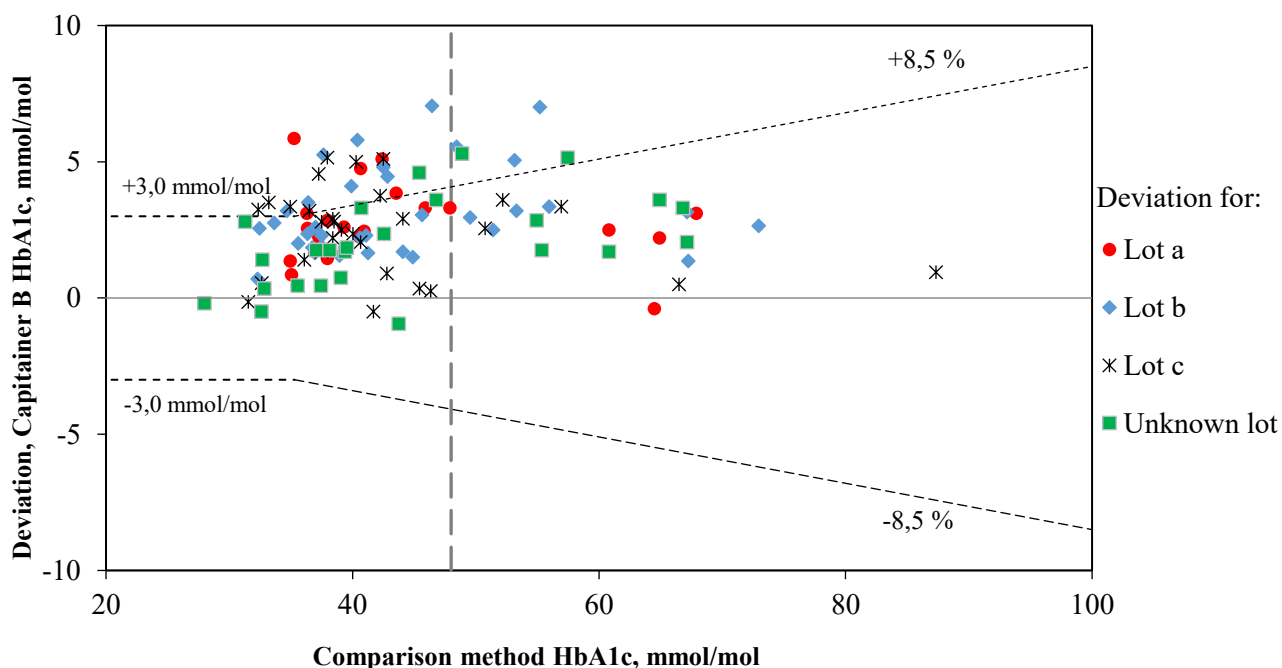


Figure 4. Accuracy of HbA1c results from Capitainer B samples when the samples were collected by health care personnel. The x-axis represents the mean HbA1c result of the comparison method. The y-axis represents the HbA1c deviation of a single Capitainer B sample measurement from the mean result of the corresponding sample of the comparison method. For the 59 samples with only a single measurement on the comparison method, the HbA1c deviation of a single Capitainer B sample measurement from the single result of the corresponding sample of the comparison method is shown. The vertical line at 48 mmol/mol HbA1c illustrates the diagnostic threshold value for diabetes. The different lots of Capitainer B are illustrated with the symbols ● (Lot a), ◆ (Lot b), ✕ (Lot c) and ■ (Unknown lot). Stippled lines represent the allowable deviation limits according to the APS (within $\pm 3,0$ mmol/mol of the results of the comparison method for HbA1c concentrations $< 35,3$ mmol/mol and within $\pm 8,5$ % for HbA1c concentrations $\geq 35,3$ mmol/mol). Number of results (n) = 111. An account of the number of samples is given in section 6.1.

Discussion

As shown in figure 4, the results from the Capitainer B samples are consequently higher than the results from the comparison method, which is in consistence with the bias (table 6). Of the 111 results, 83 were inside the limits of allowable deviation, which corresponds to 74 % within the limits. This is in line with the systematically positive bias, especially in level 1 and 2. Separate lot calculations were not performed, but visual inspection does not indicate any lot differences.

Conclusion

When Capitainer B sample was collected by health care personnel and measurements on cobas pro was performed by BLSs, the APS for accuracy was not fulfilled.

6.4. Analytical performance of Capitainer B/cobas pro system when samples collected by lay persons

The results below reflect the analytical performance of Capitainer B when the samples were collected by lay persons recruited in the PHCCs. The results may deviate from the results achieved when the samples were collected by health care personnel.

All results from the internal analytical quality control (PeciControl HbA1c Norm and Path), two levels, were within the allowable control limits (data not shown). The internal analytical quality controls were measured on Roche cobas pro c 503 with Tina-quant hemolysate application (ACN 851).

The Capitainer B samples were exposed to varying outside temperatures under transport by regular mail as the evaluation period stretched from early summer to mid fall. All Capitainer B samples collected by lay persons were measured within 14 days of collection with an average time of 8 days (data not shown).

6.4.1. The precision of Capitainer B/cobas pro system

Two measurements of the capillary whole blood sample, one from each of the sample discs of the Capitainer B, were performed. Meaning that two separate elutions were performed, one for each sample disc, so that the two measurements come from different blood drops, and separate elution wells. The results were checked visually to meet the imposed condition for using formula 1 in attachment 4. There were no systematic differences pointed out between the paired measurements (data not shown).

The precision is presented as repeatability (CV). The CV with a 90 % CI is shown in table 7. The results were sorted and divided into three concentration levels according to the mean of the results of the samples collected with Capitainer B. Raw data is attached for the requesting company only, see attachment 8.

Table 7. Repeatability (CV) of Capitainer B samples measured for HbA1c. Results achieved when the samples were collected by lay persons in PHCCs.

Level	n	Excluded results (statistical outliers)	Mean value HbA1c, mmol/mol	CV (90% CI), %
1	4*			
2	48	0	49,0	1,5 (1,3 - 1,8)
3	23	0	68,9	2,0 (1,6 - 2,7)

An account of the number of samples is given in section 6.1.

* n<8: CV not reported due to high degree of uncertainty.

Discussion

The CV achieved when sampling was performed by lay persons in PHCCs was between 1,5 and 2,0 % depending on the concentration level. The CV was statistically significantly lower than the

APS for level 2 and 3. The CV could not be reported in level 1 due to too few results and thus a high degree of uncertainty.

Conclusion

When Capitainer B samples was collected by lay persons and measurements on cobas pro was performed by BLSs, the APS for repeatability ($CV \leq 3,0\%$) was fulfilled in level 2 and 3 and not determined in level 1.

6.4.2. The bias of Capitainer B/cobas pro system

The mean deviation (bias) of Capitainer B sample results from the comparison method was calculated. The bias is presented with a 95 % CI in table 8. The results were sorted and divided into three concentration levels according to the mean results of the comparison method. Raw data is attached for the requesting company only, see attachments 6 and 8.

Table 8. Bias of Capitainer B samples measured for HbA1c. Results achieved when the samples were collected by lay persons in PHCCs.

Level	n*	Excluded results (statistical outliers)	Mean HbA1c value comparison method, mmol/mol	Mean HbA1c value Capitainer B, mmol/mol	Bias (95 % CI), mmol/mol	Bias, %
1	15	0	35,3	39,7	4,3 (3,8 — 4,8)	12,2
2	58	1**	47,8	53,4	5,7 (5,1 — 6,2)	11,9
3	16	0	66,4	72,0	5,6 (4,7 — 6,5)	8,4

*The given number of results (n) were counted before the exclusion of statistical outliers. Mean and bias were calculated after the exclusion of statistical outliers. An account of the number of samples is given in section 6.1.

**ID 1025 was a statistical outlier according to Burnett's model [11] in the calculation of bias and therefore excluded.

Discussion

There was a statistically significant bias between the Capitainer B samples and the comparison method in all concentration levels. The results from the Capitainer B samples were systematically higher than the results from the comparison method, ranging from 4,3 to 5,7 mmol/mol.

6.4.3. The accuracy of Capitainer B/cobas pro system

To evaluate the accuracy of HbA1c results on Capitainer B samples, the agreement between Capitainer B samples and the venous samples analysed on the comparison method is illustrated in a difference plot (figure 5). The limits for the allowable deviation according to the APS, within $\pm 3,0$ mmol/mol of the results of the comparison method for HbA1c concentrations $< 35,3$ mmol/mol and within $\pm 8,5\%$ for HbA1c concentrations $\geq 35,3$ mmol/mol, are shown with stippled lines. The plot includes the deviation in HbA1c concentration between the first measurement of each Capitainer B sample against the mean result of the corresponding sample of the comparison method. The plot illustrates both random and systematic errors, reflecting the

total measuring error in the results from the Capitainer B samples. Raw data is attached for the requesting company only, see attachments 6 and 8.

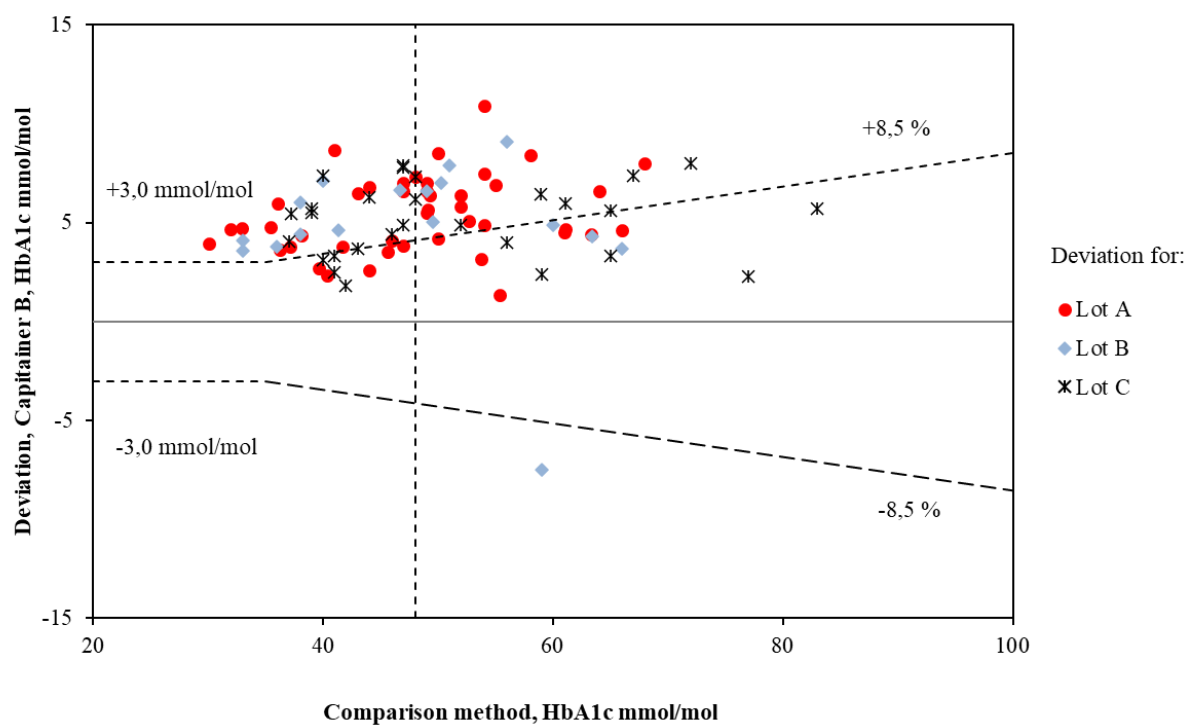


Figure 5. Accuracy of HbA1c results from Capitainer B samples when the samples were collected by lay persons. The x-axis represents the mean HbA1c result of the comparison method. The y-axis represents the HbA1c deviation of a single Capitainer B sample measurement from the mean result of the corresponding sample of the comparison method. The vertical line at 48 mmol/mol HbA1c illustrates the diagnostic threshold value for diabetes. The different lots of Capitainer B are illustrated with the symbols ● (Lot a), ◆ (Lot b) and ✱ (Lot c). Stippled lines represent the allowable deviation limits according to the APS (within $\pm 3,0$ mmol/mol of the results of the comparison method for HbA1c concentrations $< 35,3$ mmol/mol and within $\pm 8,5$ % for HbA1c concentrations $\geq 35,3$ mmol/mol). Number of results (n) = 89. An account of the number of samples is given in section 6.1.

Discussion

As shown in figure 5, the results from the Capitainer B samples are consequently higher than the results from the comparison method, which is in consistence with the bias (table 8). Of the 89 results, 24 were inside the limits of allowable deviation, which corresponds to 27 % within the limits. Separate lot calculations were not performed.

Conclusion

When Capitainer B samples was collected by lay persons and measurements on cobas pro was performed by BLSs the APS for accuracy was not fulfilled. Based on these results, the manufacturer requested the opportunity to make changes to the pre-analytical procedure and the recommended stability time of the sampling card, followed by a second evaluation (see section 7).

6.5. Deviation between Capitainer B/cobas pro system and the comparison method related to the time from sampling to analysis

The time from sampling until analysis of the Capitainer B samples was considerably different between the two evaluation settings, rendering a suspicion of a stability issue as the samples collected by health care personnel and lay persons showed significantly different bias and accuracy results. Therefore, a decision was made by SKUP to investigate if the stability could be the reason for the deviating results.

The trend in the agreement between the Capitainer B samples and the comparison method, related to the days from sampling with Capitainer B until analysis, is illustrated in the difference plot in figure 6. The plot shows the deviation between the mean HbA1c result of the Capitainer B sample and the mean HbA1c result of the corresponding sample on the comparison method. The plot includes both samples collected by lay persons at PHCCs and samples collected by health care personnel at the hospital laboratory. Raw data is attached for the requesting company only, see attachment 6, 7 and 8.

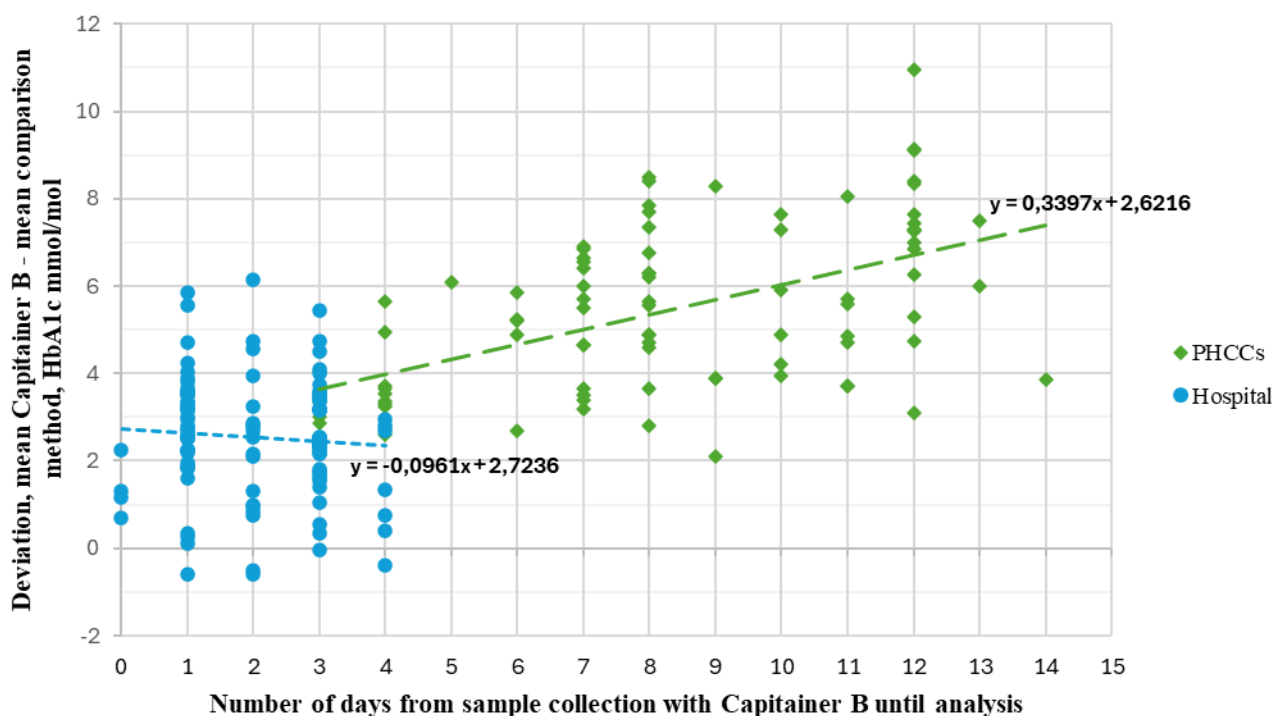


Figure 6. The plot shows the deviation between the mean result of the Capitainer B sample and the mean result of the comparison method, when collected by lay persons at PHCCs and by health care personnel at the hospital laboratory, in relation to the number of days from sample collection with Capitainer B until the analysis date. The y-axis represents the HbA1c deviation between the mean result of the Capitainer B sample and the mean result of the corresponding sample of the comparison method. For the samples where one of the duplicates was reported as missing, the deviation was calculated from only one measurement. The x-axis represents the number of days from sample collection with Capitainer B until analysis. Samples collected at the PHCCs are represented by the symbol ♦ and samples collected at the hospital laboratory are represented by the symbol ●. The stippled lines illustrate the

regression curve. ID1025 and ID34 were statistical outliers according to Burnett's model [11] and were therefore not included in the plot. Number of results (n) = 88 (PHCCs), (n) = 108 (Hospital).

The bias achieved when the samples were collected by lay persons and stratified on number of days from sampling until analysis is presented with a 95 % CI in table 9. Raw data is attached for the requesting company only, see attachment 6, 7 and 8.

Table 9. Bias of Capitainer B samples measured for HbA1c stratified on number of days from sampling until analysis. Results achieved when the samples were collected by lay persons in PHCCs.

Number of days	n	Excluded results (statistical outliers)	Mean HbA1c value comparison method, mmol/mol	Mean HbA1c value Capitainer B, mmol/mol	Bias (95 % CI), mmol/mol	Bias, %
≤7 days	35	0	47,5	51,9	4,4 (3,9 — 4,9)	9,3
>7 days	54	1*	50,1	56,2	6,1 (5,6 — 6,6)	12,2

*ID 1025 was a statistical outlier according to Burnett's model [11] in the calculation of bias and therefore excluded.

Discussion

The linear regression for the samples collected by lay persons at the PHCCs illustrates a positive increase in the deviation between the results from the Capitainer B samples and the comparison method as the number of days from sample collection to analysis increases. The linear regression shows a statistically significant slope of 0,34 (95% CI 0,22 – 0,46). The samples collected by health care personnel at the hospital laboratory were analysed within four days, and the linear regression indicates a stable deviation between the results from the Capitainer B samples and the comparison method with a slope of -0,10 (95% CI -0,35 – 0,15).

There was a statistically significant difference in bias between the Capitainer B samples analysed within 7 days after sampling compared to samples analysed more than 7 days after sampling, as the CIs of the bias did not overlap (Table 9). This indicates that the systematic deviation between the results from the Capitainer B samples and the comparison method increases with time from sampling until analysis. Based on these results, the manufacturer shortened the recommended stability time of the Capitainer B sample, and a second evaluation was performed (see section 7).

6.6. Evaluation of user-friendliness, first evaluation

6.6.1. Questionnaire to the evaluators

The most important response regarding user-friendliness comes from the intended users themselves. After sample collection, the lay persons filled in a questionnaire about the user-friendliness of sampling with Capitainer B. At the end of the evaluation period, the BLSs filled in a questionnaire about the user-friendliness of the preanalytical procedure for extraction and elution of the Capitainer B samples at the hospital laboratory. SKUP had prepared detailed instructions for this.

The questionnaire was divided into three subareas:

Tables A1 and A2 Rating of ease of operation. Is Capitainer B easy to handle?

Tables B1 and B2 Rating of the information in the instruction for use (IFU) about sample collection and insert about the elution of the samples, respectively

Table C Rating of time factors

The lay persons filled in table A1 and B1, and the BLSs collaboratively filled in table A2 and B2. SKUP filled in table C and topics marked with grey colour in table A1/A2 and B1/B2. The information in table C and the topics marked with grey colour in table A1/A2 and B1/B2 is derived from information material from the manufacturer.

In the tables, the first column shows what is up for consideration. The second column in table A1/A2 and B1/B2 shows the rating by the lay persons/ the BLSs. The rest of the columns show the rating options. The overall ratings from all the evaluating sites are marked in coloured and bold text.

The total rating is an overall assessment by SKUP of the described property, and not necessarily the arithmetic mean of the rating in the rows. Consequently, a single poor rating can justify an overall poor rating if this property seriously influences the user-friendliness of the system.

Unsatisfactory and intermediate ratings are marked with a number and explained below the tables. The intermediate category covers neutral ratings assessed as neither good nor bad.

An assessment of the user-friendliness is subjective, and the topics in the questionnaire may be emphasised differently by different users. The assessment can therefore vary between different persons and between the countries. This is discussed and taken into account in the overall assessment of the user-friendliness.

Comment

In this evaluation, the user-friendliness was assessed by 54 lay persons (A1 and B1) and by two BLSs (A2 and B2).

Questionnaire to the lay persons regarding sampling with Capitainer B:

Table A1. Rating of ease of operation.

Topic	Rating % (n)	Rating % (n)	Rating % (n)	No opinion ¹ % (n)
To prepare the sampling card	Satisfactory 83 (45)	Intermediate 0 (0)	Unsatisfactory 2 (1)	No opinion 15 (8)
To apply blood	Satisfactory 80 (43)	Intermediate 0 (0)	Unsatisfactory 5 (3)	No opinion 15 (8)
Specimen volume	Satisfactory 81 (44)	Intermediate 2 (1)	Unsatisfactory 0 (0)	No opinion 17 (9)
Design of sampling card	Satisfactory 81 (44)	Intermediate 0 (0)	Unsatisfactory 0 (0)	No opinion 19 (10)
Readability of the control window	Satisfactory 83 (45)	Intermediate 2 (1)	Unsatisfactory 0 (0)	No opinion 15 (8)
Sources of errors	Satisfactory 61 (33)	Intermediate 4 (2 ²)	Unsatisfactory 0 (0)	No opinion 35 (19)
Hygiene, when using the sampling card	Satisfactory 83 (45)	Intermediate 0 (0)	Unsatisfactory 0 (0)	No opinion 17 (9)
Intended users	Health care personnel or patients	Laboratory experienced personnel	Biomedical laboratory scientists	

Total rating by SKUP

Satisfactory

¹Participants that either have chosen the “No opinion” option in the scheme or have not given an answer to the specific question.

²The biggest risk is the handling of the test card, the well opening is too small, and the required blood volume is small. It can be challenging for a person with physical disabilities, such as tremor.

Comment on intermediate and unsatisfactory ratings of ease of operation that were not linked to a specific topic:

Good system but failed in the sampling in the second well.

Additional positive comments to the ease of operation:

Can be good for getting better control of one's long-term HbA1c value and, in that sense, easier to adjust oneself so that it becomes a better value, with e.g. diet and exercise. Easy to use. Good.

Additional negative comments to the ease of operation:

None given.

Table B1. Rating of the information in the IFU about the sample collection.

Topic	Rating % (n)	Rating % (n)	Rating % (n)	No opinion ¹ % (n)
Preparations / Pre-analytic procedure	Satisfactory 78 (42)	Intermediate 0 (0)	Unsatisfactory 0 (0)	No opinion 22 (12)
Specimen collection	Satisfactory 78 (42)	Intermediate 0 (0)	Unsatisfactory 0 (0)	No opinion 22 (12)
Readability of the control window	Satisfactory 76 (41)	Intermediate 0 (0)	Unsatisfactory 0 (0)	No opinion 24 (13)
Description of the sources of error	Satisfactory 63 (34)	Intermediate 4 (2)	Unsatisfactory 0 (0)	No opinion 33 (18)
Readability/Clarity of presentation	Satisfactory 78 (42)	Intermediate 0 (0)	Unsatisfactory 0 (0)	No opinion 22 (12)
General impression	Satisfactory 78 (42)	Intermediate 0 (0)	Unsatisfactory 0 (0)	No opinion 22 (12)
Available insert in Danish, Norwegian, Swedish	Satisfactory	Intermediate	Unsatisfactory	

Total rating by SKUP **Satisfactory**

¹Participants that either have chosen the “No opinion” option in the scheme or have not given an answer to the specific question.

Additional positive comments to the IFU:

Go, go gadget!

Additional negative comments to the IFU:

None given.

Questionnaires to the BLS's at the hospital laboratory about the pre-analytical procedure for extraction and elution of Capitainer B samples before analysis:

Table A2. Rating of ease of operation.

Topic	Rating	Rating	Rating	Rating	Option
Extraction of sample from Capitainer B	S	Satisfactory	Intermediate	Unsatisfactory	No opinion
To prepare the sample	S, I ¹	Satisfactory	Intermediate	Unsatisfactory	No opinion
Specimen volume	S, I ²	Satisfactory	Intermediate	Unsatisfactory	No opinion
Number of procedure step, for elution and preparation	S	Satisfactory	Intermediate	Unsatisfactory	No opinion
Design of sampling card	S	Satisfactory	Intermediate	Unsatisfactory	No opinion
Sources of errors	I ³	Satisfactory	Intermediate	Unsatisfactory	No opinion
Hygiene, when using the test	S	Satisfactory	Intermediate	Unsatisfactory	No opinion
Environmental aspects: waste handling		No precautions	Sorted waste	Special precautions	
Total rating by SKUP		Satisfactory			

¹Some filters become static, which means it requires a tool or finger to push the sample filter down into the tube. It gets stuck on the tweezers.

²A little too many participants did not succeed in getting a sufficient amount of blood in the filter.

³Too little blood /too low blood volume. Other than that, I recognize that there are few sources of errors, as even too low blood volume gives a result. It seems that as long as the filter turns red, it is enough blood.

Additional positive comment to the ease of operation:

Easy to analyse the sampling card.

Additional negative comments to the ease of operation:

None given.

Table B2. Rating of the information in the insert about the elution of the samples.

Topic	Rating	Rating	Rating	Rating	Option
Preparations / Pre-analytic procedure	S, I ¹	Satisfactory	Intermediate	Unsatisfactory	No opinion
Description of the sources of error	S	Satisfactory	Intermediate	Unsatisfactory	No opinion
Readability/Clarity of presentation	S	Satisfactory	Intermediate	Unsatisfactory	No opinion
General impression	S	Satisfactory	Intermediate	Unsatisfactory	No opinion
Available insert in Danish, Norwegian, Swedish		Satisfactory	Intermediate	Unsatisfactory	
Total rating by SKUP		Satisfactory			

¹Could be written more clearly, but it is understandable.

Additional positive comment to the insert:
Straight forward.

Additional negative comments to the insert:
None given.

Table C. Rating of time factors. Information derived from the IFU and attachment 1 (rated by SKUP)

Topic	Rating	Rating	Rating
Required training time, self-sampling	<2 hours	2 to 8 hours	>8 hours
Storage conditions for sampling card, unopened package	+15 to +30°C	+2 to +8°C	−20°C
Storage conditions for sampling cards, opened package	+15 to +30°C or disposable	+2 to +8°C	−20°C
Stability of sample card, unopened package	>5 months	3 to 5 months	<3 months
Stability of sample card, opened package	>30 days or disposable	14 to 30 days	<14 days
Total rating by SKUP		Satisfactory	

6.6.2. Assessment of the user-friendliness

Assessment of the ease of operation by the intended users (table A1)

The ease of operation was in total assessed as satisfactory by the lay persons, but there were some intermediate and unsatisfactory ratings. The motivations for the lower ratings were based on handling of the sampling card, especially regarding applying the blood to the filter/well. There were also positive comments regarding easy handling and that the sampling card could be beneficial in long term monitoring of HbA1c.

Assessment of the information in the IFU by the intended users (table B1)

The IFU was assessed as satisfactory by the lay persons with only a few intermediate ratings.

Assessment of the ease of operation for pre-analytical procedure by experienced laboratory personnel (table A2)

Assessment of the ease of operation for pre-analytical procedure was in total assessed as satisfactory by the BLSs, but there were some intermediate ratings. The motivations for the lower ratings were based on handling of the filters (transfer to tubes) and that some filters did not have sufficient amount of blood. There was also given a positive comment regarding the easiness of the analysis.

Assessment of the information in the insert for pre-analytical procedure by BLSs (table B2)

The insert for pre-analytical procedure for use was assessed as satisfactory by the BLSs with a one intermediate ratings, regarding the clarity of the text. One positive comment was given regarding easiness of the pre-analytical procedure.

Assessment of internal quality control and stability (table C)

The internal quality control and test stability were assessed as satisfactory.

Conclusion

In all, the user-friendliness of Capitainer B and the pre-analytical procedure and their instruction of use, was rated as satisfactory, although there is improvement potential pointed out in the comments. The performance specification for user-friendliness was fulfilled.

7. Second evaluation after changes made by the manufacturer

7.1. Background

After completing the first evaluation of Capitainer B sampling card, Capitainer AB asked for the opportunity to make changes to the pre-analytical procedure and the recommended stability time of the Capitainer B sample in response to initial poor accuracy in the first evaluation. In accordance with SKUP's policy, a second evaluation of the analytical performance (precision and accuracy) in the hands of the intended users of the Capitainer B sampling card was performed before publishing the results from the first evaluation, as the sampling card had not previously been used for HbA1c measurements in the Scandinavian market.

7.2. The model of the evaluation of Capitainer B

The second evaluation included only the part related to Capitainer B samples collected by lay persons with diabetes recruited at PHCCs, and in addition the evaluating BLSs in the hospital laboratory assessed the user-friendliness, as the pre-analytical procedure had been changed by the manufacturer. In the second evaluation, the venous blood samples for the comparison method were only measured once as the first evaluation demonstrated high precision of duplicate measurements at all concentration levels, see table 3.

7.3. Materials and methods

Capitainer AB made changes to the pre-analytical procedure and the handling of the Capitainer B sampling card. The changes are listed below.

- The Capitainer B sampling card should be analysed within 5 days after sampling.
- The Capitainer B sampling card should be shipped individually, with one sampling card per envelope.
- The pre-analytical protocol for Roche Tina-Quant HbA1c, developed by Capitainer AB, was adjusted. See attachment 5 for details.

7.3.1. The second evaluation

Inquiry about an evaluation

Capitainer AB via Mikael Ström, Business Development Manager, applied to SKUP in December 2024 for a second evaluation of Capitainer B during their work with procedural changes. This was in response to the initial poor accuracy, as the results from the Capitainer B samples collected by lay persons at the PHCCs were systematically higher than the results from the corresponding venous samples from the comparison method in the first evaluation.

Protocol, arrangements and contract

In March 2025, the changes were implemented and the protocol for the evaluation was approved, and Capitainer AB and SKUP signed a contract for the evaluation. The same hospital laboratory as in the first evaluation, Laboratory medicine at Östersund Hospital, Sweden, was assigned to do the practical work with the Capitainer B samples and the comparison method. Seven PHCCs in Region Jämtland Härjedalen, Sweden, agreed to recruit participants for the evaluation; Brunflo hälsocentral, Frösö hälsocentral, Funäsdalens hälsocentral, Odensala hälsocentral, Strömsunds hälsocentral, Svegs hälsocentral, Zätaagränds hälsocentral

Training

Capitainer AB was responsible for the necessary training for the changed pre-analytical procedure among BLSs at the hospital laboratory. The training was given digitally in the local language.

Timeline of the practical work

The practical work was carried out over 15 weeks, ending in July 2025.

7.4. Results and discussion, second evaluation

7.4.1. Number of samples

The scheduled number of samples in this evaluation was 90 participant samples collected in duplicate at the PHCCs and measured at the hospital laboratory. In the end the PHCCs collected samples from 115 participants. The results from the comparison method covered the HbA1c interval 24 – 85 mmol/mol. The evaluation was carried out using four lot numbers of Capitainer B. An account of the number of samples not included in the calculations is given below.

Missing results

- No SKUP ID; 23 duplicated results were reported as missing due to unsuccessful sample collection in both wells of the Capitainer B samples.
- For 10 of the Capitainer B samples, one of the duplicated results from each sampling card were reported as missing due to unsuccessful sample collection in the second well (IDs, see attachment 6). The single measurements were included in the calculation of bias and the assessment of accuracy but not included in the calculation of Capitainer B repeatability.
- ID 2033, 2034; one of the results from the Capitainer sample was reported as missing due to incorrect handling of the sample at the laboratory. The single measurements were included in the calculation of bias and the assessment of accuracy but not included in the calculation of Capitainer B repeatability.

Omitted results

- ID 2009, 2030, 2047-2051, 2055, 2056, 2058, 2073, 2074, 2076, 2077, 2084 and 2086-2092 (samples from 22 participants); were omitted as the Capitainer B samples had exceeded the manufacturer recommended stability time when arriving at the hospital laboratory. For 5 of these participants, one of the duplicated results were also reported as missing due to unsuccessful sample collection in the second well.

Excluded results (statistical outliers)

Statistical outliers in SKUP evaluations are detected by the criterion promoted by Burnett [11]. Statistical outliers:

- ID 2075; the results from the Capitainer B sample were classified as outliers according to Burnett's model in the calculation of repeatability and therefore not included in the calculation of repeatability and bias of Capitainer B but were included in the assessment of accuracy (the first of the duplicate measurements).

7.4.2. Analytical performance of the selected comparison method

7.4.2.1. Internal analytical quality control

All results from the internal analytical quality controls (PeciControl HbA1c Norm and Path), two levels, were within the allowable control limits (data not shown). The internal analytical quality controls were measured on Roche cobas pro c 503 with Tina-quant whole blood application (ACN 881).

7.4.2.2. The precision of the comparison method

The precision was not determined during the second evaluation as only single measurements of the venous whole blood sample were performed on the comparison method. Raw data is attached for the requesting company only, see attachment 9.

7.4.2.3. The trueness of the comparison method

The trueness of the comparison method was verified with EQA results. The results from three HbA1c EQA surveys from Equalis (specified in section 5.3.1) are shown in table 10.

Table 10. EQA control material from Equalis measured on the comparison method.

Period of survey	Assigned value, HbA1c mmol/mol (acceptance limits)	n	Result cobas pro c 503, HbA1c mmol/mol
2025:04	43,0 ± 3,27 (39,73 – 46,27)	1	44,3
2025:05	47,6 ± 3,46 (44,14 – 51,06)	1	46,6
2025:06	46,2 ± 3,41 (42,79 – 49,61)	1	44,5

Discussion

The trueness of the comparison method was confirmed by the results in the national EQA scheme for HbA1c.

7.4.3. Analytical performance of Capitainer B/cobas pro system when samples collected by lay persons

The internal analytical quality controls were measured on Roche cobas pro c 503 with Tina-quant hemolysate application (ACN 851). All results from the internal analytical quality control (PeciControl HbA1c Norm and Path), two levels, were within the allowable control limits (data not shown), except for one day, when the result from the PeciControl Path was below the allowable control limit. Despite this, it was decided to include the Capitainer B sample results from that day.

All Capitainer B samples collected by lay persons included in the calculations were measured within five days of collection (data not shown).

7.4.3.1. The precision of Capitainer B/cobas pro system

Two measurements of the capillary whole blood sample, one from each of the sample wells of the Capitainer B, were performed. The results were checked visually to meet the imposed condition for using formula 1 in attachment 4. There were no systematic differences pointed out between the paired measurements (data not shown).

The precision is presented as repeatability (CV). The CV with a 90 % CI is shown in table 11. The results were sorted and divided into three concentration levels according to the mean of the results of the samples collected with Capitainer B. Raw data is attached for the requesting company only, see attachment 10.

Table 11. Repeatability (CV) of Capitainer B samples measured for HbA1c. Results achieved when the samples were collected by lay persons in PHCCs in the second evaluation.

Level	n*	Excluded results (statistical outliers)	Mean value HbA1c, mmol/mol	CV (90% CI), %
1	11	0	36,2	1,3 (1,0 - 2,1)
2	39	1**	46,0	0,8 (0,6 - 0,9)
3	8	0	69,6	1,0 (0,7 - 1,7)

*An account of the number of samples is given in section 7.4.1.

***ID 2075 was a statistical outlier according to Burnett's model [11] and therefore excluded.

Discussion

The CV achieved when sampling was performed by lay persons in PHCCs was between 0,8 and 1,3 % depending on the concentration level. The CV was statistically significantly lower than the APS for all levels.

Conclusion

When Capitainer B samples was collected by lay persons and measurements on cobas pro was performed by BLSSs, the APS for repeatability ($CV \leq 3,0$ %) was fulfilled in all levels in the second evaluation.

The results demonstrated improved repeatability in level 2 and 3 compared to the first evaluation. CV for level 1 was not comparable as it was not reported for level 1 in the first evaluation, see table 7.

7.4.3.2. The bias of Capitainer B/cobas pro system

The mean deviation (bias) of Capitainer B sample results from the comparison method was calculated. The bias is presented with a 95 % CI in table 12. The results were sorted and divided into three concentration levels according to the result of the comparison method. Raw data is attached for the requesting company only, see attachments 9 and 10.

Table 12. Bias of Capitainer B samples measured for HbA1c. Results achieved when the samples were collected by lay persons in PHCCs in the second evaluation.

Level	n*	Excluded results (statistical outliers)	Mean HbA1c value comparison method, mmol/mol	Mean HbA1c value Capitainer B, mmol/mol	Bias (95 % CI), mmol/mol	Bias %
1	14	0	35,3	37,1	1,8 (0,9 — 2,7)	5,1
2	48	0	45,9	47,9	2,1 (1,5 — 2,7)	4,5
3	7	0	73,3	74,0	0,7 (-0,9 — 2,3)	1,0

*An account of the number of samples is given in section 6.1.

Discussion

There was a statistically significant bias between the Capitainer B samples and the comparison method in concentration level 1 and 2, where the results from the Capitainer B samples were systematically higher by 1,8 and 2,1 mmol/mol, respectively. The results demonstrated a lower bias in all levels compared to the first evaluation.

7.4.3.3. The accuracy of Capitainer B/cobas pro system

To evaluate the accuracy of HbA1c results on Capitainer B samples, the agreement between Capitainer B samples and the venous samples analysed on the comparison method is illustrated in a difference plot (figure 7). The limits for the allowable deviation according to the APS, within $\pm 3,0$ mmol/mol of the results of the comparison method for HbA1c concentrations $< 35,3$ mmol/mol and within $\pm 8,5$ % for HbA1c concentrations $\geq 35,3$ mmol/mol, are shown with stippled lines. The plot includes the deviation in HbA1c concentration between the first measurement of each Capitainer B sample against the result of the corresponding sample of the comparison method. The plot illustrates both random and systematic errors, reflecting the total measuring error in the results from the Capitainer B samples. Raw data is attached for the requesting company only, see attachments 9 and 10.

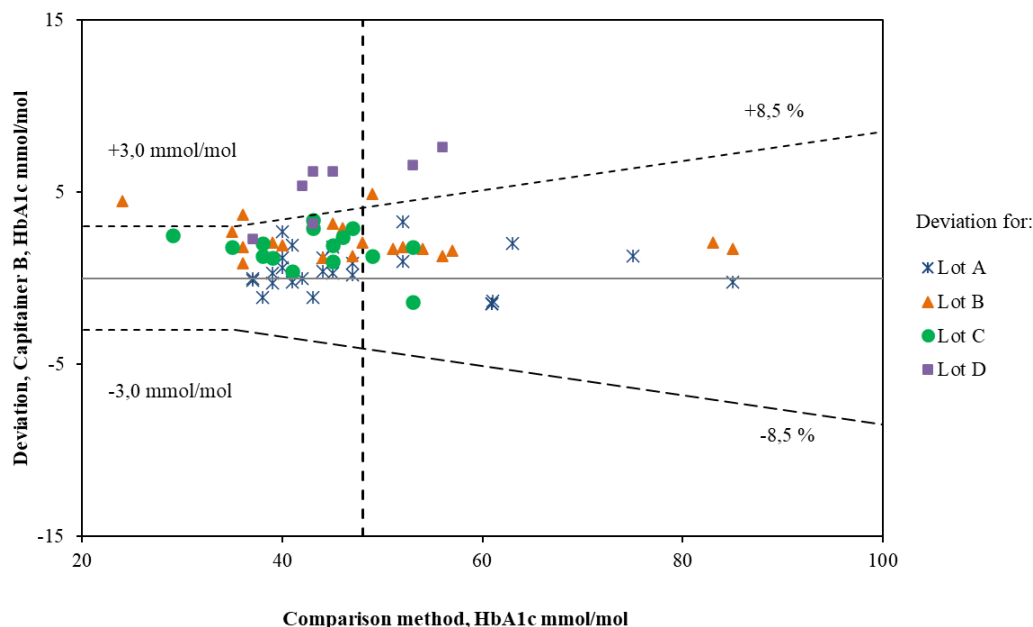


Figure 7. Accuracy of HbA1c results from Capitainer B samples when the samples were collected by lay persons in the second evaluation. The x-axis represents the HbA1c result of the comparison method. The y-axis represents the HbA1c deviation of the first Capitainer B sample measurement from the result of the corresponding sample of the comparison method. The vertical line at 48 mmol/mol HbA1c illustrates the diagnostic threshold value for diabetes. The different lots of Capitainer B are illustrated with the symbols * (Lot a), ▲ (Lot b), ● (Lot c) and ■ (Lot d). Stippled lines represent the allowable deviation limits according to the APS (within $\pm 3,0$ mmol/mol of the results of the comparison method for HbA1c concentrations $< 35,3$ mmol/mol and within $\pm 8,5$ % for HbA1c concentrations $\geq 35,3$ mmol/mol). Number of results (n) = 70. An account of the number of samples is given in section 6.1.

Discussion

Of the 70 results, 62 were inside the limits of allowable deviation, which corresponds to 89 % within the limits. Separate lot calculations were not performed. Lot D showed 5 of 8 results above the upper limit, indicating poorer quality compared to the other lots. Lot D was analysed on a day when the internal quality control result from PreciControl Path was below the allowable control limit, indicating that the results could be too low, but in fact the Lot D results were too high.

Conclusion

When Capitainer B samples were collected by lay persons and measurements on cobas pro were performed by BLSSs, the APS criterion for accuracy was not fulfilled in the second evaluation. However, the results demonstrated clearly improved accuracy compared to the first evaluation, with only 27 % of measurements being within the specified limits.

7.4.4. Evaluation of user-friendliness, second evaluation

7.4.4.1. Questionnaire to the evaluators

At the end of the evaluation period, the same two BLSs collaboratively filled in the same questionnaire as in the first evaluation, tables A3 and B3. As the procedure for sampling with Capitainer B had not changed, it was not necessary to repeat the evaluation of user-friendliness by lay persons.

Table A3 Rating of ease of operation. Is Capitainer B easy to handle?

Table B3 Rating of the insert about the elution of the samples

In tables A3 and B3, the questions related to the changes in the pre-analytical procedure for extraction and elution are written in bold. These questions had most impact on the total rating by SKUP in the second evaluation.

Questionnaire to the BLS's at the hospital laboratory about the pre-analytical procedure for extraction and elution of Capitainer B samples before analysis:

Table A3. Rating of ease of operation.

Topic	Rating	Rating	Rating	Rating	Option
Extraction of sample from Capitainer B	S	Satisfactory	Intermediate	Unsatisfactory	No opinion
To prepare the sample	S	Satisfactory	Intermediate	Unsatisfactory	No opinion
Specimen volume	U¹	Satisfactory	Intermediate	Unsatisfactory	No opinion
Number of procedure step, for elution and preparation	S	Satisfactory	Intermediate	Unsatisfactory	No opinion
Design of sampling card	S	Satisfactory	Intermediate	Unsatisfactory	No opinion
Sources of errors	I²	Satisfactory	Intermediate	Unsatisfactory	No opinion
Hygiene, when using the test	S	Satisfactory	Intermediate	Unsatisfactory	No opinion
Total rating by SKUP		Satisfactory			

¹Since many wells were not filled, some had one or none, a thorough training of the patient is required if they are to perform self-testing at home. 10 microliters is a lot of blood if you're not used to pricking yourself.

²Too little sample in the wells, patient training is needed. Do not send cards over the weekend, sample collection should be done Monday to Wednesday.

Additional positive comment to the ease of operation:

None given.

Additional negative comments to the ease of operation:

None given.

Table B3. Rating of the information in the insert about the elution of the samples.

Topic	Rating	Rating	Rating	Rating	Option
Preparations / Pre-analytic procedure	S, I ¹	Satisfactory	Intermediate	Unsatisfactory	No opinion
Description of the sources of error	S, I ²	Satisfactory	Intermediate	Unsatisfactory	No opinion
Readability/Clarity of presentation	S	Satisfactory	Intermediate	Unsatisfactory	No opinion
General impression	S, I ³	Satisfactory	Intermediate	Unsatisfactory	No opinion
Total rating by SKUP		Satisfactory			

¹Intermediate due to many patients failing the sampling. Sampling is considered part of the pre-analytical phase.

²Sources of error in patient instructions – they do not exist. Sources of error in the method are also not well described.

³Intermediate because the amount of blood required from the patient is quite large. It should be made even clearer that the blood must drip into the well – the patient must not touch the well with their finger.

Additional positive comment to the insert:

None given.

Additional negative comments to the insert:

None given.

7.4.4.2 Assessment of the user-friendliness

Assessment of the ease of operation for pre-analytical procedure by experienced laboratory personnel (table A3)

Overall, the ease of operation for the pre-analytical procedure was assessed as satisfactory by the BLSs. However, one intermediate and one unsatisfactory rating were reported. The reasons for these lower ratings were related to the large blood volume required, which resulted in unfilled wells, and the limited recommended stability time of the Capitainer B sampling card after collection, which posed challenges for shipment over weekends.

Assessment of the information in the insert for pre-analytical procedure by BLSs (table B3)

The insert for pre-analytical procedure for use was assessed as satisfactory by the BLSs with some intermediate ratings, regarding that many patients failing the sampling, the large blood volume required, and the insert missing a description of errors.

Conclusion

In all, the user-friendliness the pre-analytical procedure was rated as satisfactory, although there is improvement potential pointed out in the comments. The questions related to the changes in the pre-analytical procedure for extraction and elution had most impact on the total rating in the second evaluation. The performance specification for user-friendliness of the pre-analytical procedure was fulfilled.

8. References

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Attachments

1. Facts about Capitainer B
2. Information about manufacturer, retailers and marketing
3. Product specifications for this evaluation, Capitainer B
4. Statistical expressions and calculations
5. Pre-analytical protocol for Roche Tina-Quant HbA1c and hemolysate application from Capitainer®B.
6. First evaluation - Raw data HbA1c, results from the comparison method
7. First evaluation - Raw data HbA1c, Capitainer B results, hospital
8. First evaluation - Raw data HbA1c, Capitainer B results, lay persons
9. Second evaluation - Raw data HbA1c, results from the comparison method
10. Second evaluation - Raw data HbA1c, Capitainer B results, lay persons
11. Comments from Capitainer AB

Attachments with raw data are included only in the copy to Capitainer AB

Facts about Capitainer B

This form is filled in by Capitainer AB.

Table 1. Facts about the test kit

Name of system	Capitainer B
Number of tests in package	N/A
Package contents	Capitainer®B is delivered in packs of 50 devices, or as procedure sampling packs with one device and accessories for sampling
Measurand	N/A
Sample material	Whole blood as a volumetrically dried microsample
Sample volume	10 µL
Sampling principle	Volumetric collection of dried capillary blood
Haematocrit range:	25-55 % (Capitainer®B sampling validated range)
Limit of quantification	N/A
Test interpretation	N/A
Measurement time	N/A
Operating conditions	Temperature: 15°C to 35°C. Relative humidity: 15% to 90%. Haematocrit: 25% to 55%.
Necessary equipment not included in the package	If provided in complete self-sampling procedure packs, all components for sampling included. For 50 packs of only the cards, additional components needed are: Gauze pad, plaster, disinfection swab, lancet and return pouch.
Storage temperature	Room temperature
Stability unopened sampling card	18 months from production date
Stability opened sampling card	Sampling to be performed within 30 minutes after opening the package.
Stability of sampling card, with sample, for measurement of HbA1c	5 days

Information about manufacturer, retailers and marketing

This form is filled in by Capitainer AB.

Table 1. Marketing information

Manufacturer:	Capitainer AB
Retailers in Scandinavia:	Denmark: You Do Bio Norway: Capitainer AB Sweden: Capitainer AB
In which countries is the system marketed:	Globally ☒ Scandinavia ☐ Europe ☐
Date for start of marketing the system in Scandinavia:	2020-02
Date for CE-marking:	2022-05-25 (New CE for IVDR registered)
In which Scandinavian languages is the manual available:	All languages

Product specification of this product, Capitainer B sampling card

Capitainer B sampling cards and drying pouches used in the first evaluation.

Lot no.	Alias	Expiry date	Used by
800910	A	2025-09-30	Hospital and PHCC1
800835	B	2025-07-31	Hospital and PHCC2
800892	C	2025-08-31	Hospital and PHCC3

Capitainer B sampling cards and drying pouches used in the second evaluation.

Lot no.	Alias	Expiry date	Used by
800892	A	2025-08-31	PHCC 1-7
800910	B	2025-09-30	PHCC 1-7
801095	C	2026-05-31	PHCC 1-7
801314	D	2026-06-30	PHCC 1-7

Statistical expressions and calculations

This attachment with standardised text deals with the statistical expressions and calculations used by SKUP. The statistical calculations will change according to the type of evaluation. The descriptions in this document are valid for evaluations of quantitative methods with results on the ratio scale.

Statistical terms and expressions

The definitions in this section come from the International Vocabulary of Metrology - Basic and general concepts and associated terms; VIM [a].

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, 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.

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, poor e.g.), whereas the bias is reported in the same unit as the analytical result or in percent.

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. Accuracy is descriptive in general terms (good, poor e.g.). A measurement is said to be more accurate when it offers a smaller measurement error. Accuracy can be illustrated in a difference plot.

- a. International vocabulary of metrology – Basic and general concepts and associated terms, VIM, 3rd edition, JCGM 200;2012. www.bipm.org

Statistical calculations

Statistical outliers

The criterion promoted by Burnett [b] 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.

Calculation of imprecision

The precision of the evaluated method is assessed by use of paired measurements of genuine patient sample material. The results are usually divided into three concentration levels, and the estimate of imprecision is calculated for each level separately, using the following formula [c,d,e]:

$$SD = \sqrt{\frac{\sum d^2}{2n}} \quad \begin{array}{l} d = \text{difference between two paired measurements} \\ n = \text{number of differences} \end{array} \quad (\text{formula 1})$$

This formula is used when the standard deviation can be assumed reasonable constant across the concentration interval. If the coefficient of variation is more constant across the concentration interval, the following formula is preferred:

$$CV = \sqrt{\frac{\sum (d/m)^2}{2n}} \quad m = \text{mean of paired measurements} \quad (\text{formula 2})$$

The two formulas are based on the differences between paired measurements. The calculated standard deviation or CV is still a measure of the imprecision of single values. The imposed condition for using the formulas is that there is no systematic difference between the 1st and the 2nd measurement of the pairs. The CV is given with a 90 % confidence interval.

Calculation of bias

The mean deviation (bias) at different concentration levels is calculated. A paired t-test is used with the mean values of the duplicate results on the comparison method and the mean values of the duplicate results on the evaluated method. The mean difference is shown with a 95 % confidence interval.

Assessment of accuracy

The agreement between the evaluated method 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 evaluated method and the mean value of the duplicate results on the comparison method. The number of results within the analytical performance specification limits is counted and assessed.

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Pre-analytical protocols for Roche Tina-Quant HbA1c, and hemolysate application from *Capitainer®B*.

Protocol used in the first evaluation [a]

Place one Capitainer®B sample disc in a 5 mL tube

Add 100 µL PBS (+4°C or RT)

Incubate for 30 minutes at 300 rpm on an orbital shaker in RT.

Add 900 µL Hemolysing Reagent for Tina-Quant HbA1c (#11488457122)

Incubate for 30 minutes at 300 rpm on an orbital shaker in RT.

Use the eluate on the Roche Tina-Quant hemolysate application*.

*With this application, all samples need to be hemolyzed offline of the system.
This step is in the above protocol integrated in the elution step from *Capitainer®B*.

Protocol used in the second evaluation after changes made by the manufacturer

1. Remove the Capitainer®B sample discs with a tweezer and place each individual disc in an empty 5 mL tube.
2. Add 100 µL of PBS to each tube and cover the tubes with parafilm or a stopper to prevent evaporation.
3. Incubate the tubes during shaking at 1000 rpm for 30 minutes.
4. After the first PBS elution, add 900 µL of homolysing reagent that has reached room temperature. This step must be performed within 30 minutes from completion of the PBS elution step.
5. Incubate the tubes during shaking at 1000 rpm for 30 minutes and cover the tubes with parafilm or a stopper to prevent evaporation.
6. Place the tubes on cobas pro to analyse HbA1c using the Roche Tina-Quant hemolysate application*, the disc can be in the tube during analysis. The measurement needs to be started within 1 hour after the elution has been completed.

* This application requires pre-hemolysis of all samples before analysis. By following the pre-analytical procedure for Capitainer®B, a pre-hemolysis step similar but not identical to the original Roche protocol, is included in the elution process.

- a. Rollborn, N., Larsson, A., & Kultima, K. Analysis of HbA1c using microfluidic card (Capitainer qDBS card) as a pre-step before determination of the HbA1c value with an immunological method. *Scandinavian Journal of Clinical and Laboratory Investigation*, 2024; 84(1), 11–15.

First evaluation - Raw data HbA1c, results from the comparison method

Raw data are included only in the copy to Capitainer AB

First evaluation - Raw data HbA1c, Capitainer B results, collected by health care personnel

Raw data are included only in the copy to Capitainer AB

First evaluation - Raw data HbA1c, Capitainer B results, collected by lay persons

Raw data are included only in the copy to Capitainer AB

Second evaluation - Raw data HbA1c, results from the comparison method

Raw data are included only in the copy to Capitainer AB

Second evaluation - Raw data HbA1c, Capitainer B results, collected by lay persons

Raw data are included only in the copy to Capitainer AB

Comments from Capitainer AB



October 20th, 2025

Dear Sir/Madam,

Comments on the SKUP Evaluation of using Capitainer®B Sampling Card for HbA1c Testing on cobas® Using a Predefined Pre-Analytical Protocol

Capitainer AB thanks SKUP for its thorough evaluation of our self-sampling method for HbA1c analysis using the Roche cobas® TinaQuant assay.

Capitainer® allows individuals to easily collect blood samples at home and send them to a lab for testing. HbA1c is one of several analytes that can be measured using this collection method. We are pleased to note that our device meets the performance criteria for both user-friendliness and repeatability.

Regarding the analytical performance of the HbA1c test, we acknowledge room for improvement and that certain considerations must be taken into account when using *Capitainer*® dried blood samples with the Roche cobas® TinaQuant assay:

- A positive bias has been observed, increasing with storage beyond five days. This effect is not unique to Capitainer, but has been previously reported in relation to dried blood and HbA1c analysis.
- Limiting the time between sampling and analysis to a maximum of five days, as demonstrated in the second evaluation, significantly reduces this bias. It is therefore important to avoid extended delays between sample collection and analysis.

Capitainer will continue to investigate and develop pre-analytical storage conditions aimed at improving the stability of HbA1c in dried blood over time.

We also note that applying a correction factor for observed bias on dried blood would enhance accuracy and ensure compliance with allowable deviation limits.

Sincerely

A handwritten signature in blue ink that reads "Mikael Ström".

Mikael Ström

Business Development Director

Capitainer AB