Xprecia Stride™ Coagulation system

A system for measurement of P—Prothrombin time (INR)
manufactured by Siemens Healthcare Diagnostics INC

Report from the evaluation SKUP/2016/110

organised by SKUP at the request of Siemens Healthcare Diagnostics AS

SKUP in Denmark, Dept. KBA, Nordsjællands Hospital, 3400 Hillerød, Phone +45 4829 4176, www.skup.nu
SKUP in Norway, Noklus, Box 6165, NO-5892 Bergen, Phone +47 55979502, www.skup.nu
SKUP in Sweden, Equalis, Box 977, SE-751 09 Uppsala, Phone: +46 18 490 31 44, www.skup.nu

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

SKUP in Denmark
Under reorganisation

SKUP in Norway
Grete Monsen
Anne Christin Breivik
Marianne Risa
Sverre Sandberg
Noklus
Boks 6165
NO-5892 Bergen
+47 55 97 95 02
grete.monsen@noklus.no
anne.breivik@noklus.no
marianne.risa@noklus.no
sverre.sandberg@noklus.no

SKUP in Sweden
Elisabet Eriksson Boija
Gunnar Nordin
Equalis AB
Box 977
SE-751 09 Uppsala
+46 18 490 31 44
elisabet.eriksson.boija@equalis.se
gunnar.nordin@equalis.se

www.SKUP.nu

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The report was written by SKUP, spring 2016. Main author was Anne Christin Breivik, SKUP in Norway. In order to use the SKUP name in marketing, it has to be referred to www.skup.nu and to the report code in question; SKUP/2016/110. For more details, see attachment 1.

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Attachments with raw data are included only in the copy to Siemens Healthcare Diagnostics AS.

1. Summary

Background
Xprecia Stride™ Coagulation system is an in vitro diagnostic device for determination of prothrombin time, PT (INR). The product is intended for professional use. The sample material is fresh capillary whole blood. The system is produced by Siemens Healthcare Diagnostics INC. The system was launched into the Scandinavian market autumn 2015. The SKUP evaluation was carried out from December 2015 to March 2016 at the request of Siemens Healthcare Diagnostics AS in Norway.

The aim of the evaluation
The aim of the evaluation was to assess the analytical quality and user-friendliness of Xprecia Stride, both when used under optimal conditions by experienced laboratory personnel and when used under real-life conditions by the intended users in primary health care. The analytical results were assessed according to pre-set quality goals.

Materials and methods
Under optimal conditions capillary samples from 101 patients were measured on the Xprecia Stride (modified Quick method). In each of two primary health care centres (PHCCs), capillary samples from 40 patients were measured on Xprecia Stride. Venous samples from the same patients were analysed on a comparison method (Owren's method, STA-R Evolution, STAGO). The quality goal was a repeatability (CV) ≤5,0% and for accuracy that ≥95% of the results should be within ±20% from the results of the comparison method. The quality goal for the user-friendliness was a total rating of "satisfactory".

Results
At PT (INR) level <2,5, the CV under optimal conditions was 4,7% and under real-life conditions 4,5% and 5,5%, at the two PHCCs respectively. For PT (INR) results ≥2,5, the CV under optimal conditions was 5,3%, and under real-life conditions 6,4% and 7,1%. A negative bias ((-0,09) – (-0,17) INR) between Xprecia Stride and the comparison method was shown both under optimal conditions and under real-life conditions at PT (INR) level <2,5. At PT (INR) level ≥2,5 a bias of -0,23 INR was found in one of the PHCCs. Under optimal conditions, 93% of the results were within the quality goal for accuracy and when handled by the intended users, 92% of the results were within the quality goal for accuracy. The user-friendliness was rated as satisfactory. The fraction of tests wasted caused by technical errors was 0,3%.

Conclusion
The overall CV was just above 5%, and the quality goal for repeatability was not fulfilled. The quality goal for accuracy was not fulfilled. The quality goal for user-friendliness was fulfilled.

Comments from Siemens Healthcare Diagnostics INC
A letter with comment from Siemens Healthcare Diagnostics INC is attached to the report.

2. Abbreviations and Acronyms

BLS	Biomedical Laboratory Scientist
CI	Confidence Interval
C-NPU	The committee on Nomenclature, Properties and Units
CV	Coefficient of Variation
DEKS	Danish Institute of External Quality Assurance for Laboratories in Health Care
EQA	External Quality Assessment
Equalis	External quality assessment for clinical laboratory investigations in Sweden
ISO	The International Organization for Standardization
NKK	Norwegian Clinical Chemistry EQA Program
Noklus	Norwegian Quality Improvement of Primary Care Laboratories
PHCC	Primary health care centre
PT (INR)	Prothrombin Time International Normalized Ratio
RBT	Rabbit Brain Thromboplastin
SKUP	Scandinavian evaluation of laboratory equipment for primary health care
WHO	World Health Organization

3. Introduction

3.1. Background for the evaluation

Xprecia Stride™ Coagulation system is produced by Siemens Healthcare Diagnostics INC. The system was launched into the Scandinavian market autumn 2015. Siemens Healthcare Diagnostics AS is the requesting company in this evaluation.

3.2. The aim of the evaluation

The aim of the evaluation was to assess the analytical quality and user-friendliness of Xprecia Stride, both when used under optimal conditions by experienced laboratory personnel and when used under real-life conditions by the intended users in primary health care.

The evaluation includes:

- Examination of the analytical quality (precision and accuracy) under optimal conditions
- Examination of the analytical quality (precision and accuracy) in the hands of intended users
- Evaluation of the user-friendliness of Xprecia Stride and it's manual

3.3. The SKUP model

SKUP evaluations for quantitative methods are based upon the fundamental guidelines in a book concerning evaluations of laboratory equipment in primary health care [1]. The organisation of SKUP is described in attachment 1.
A complete SKUP evaluation consists of two parts. One part of the evaluation is carried out under optimal conditions by experienced laboratory personnel. This part documents the quality of the system under conditions as favourable as possible for achieving good analytical quality. The other part of the evaluation is carried out by intended users in at least two primary health care centres (PHCCs). This part documents the quality of the system under real-life conditions.

The evaluation under optimal conditions includes:

- Repeatability with 100 patient samples
- Comparison with an established hospital laboratory method

The evaluation performed by the intended users includes:

- Repeatability with 40 patient samples at each of the primary health care centres
- Comparison with an established hospital laboratory method
- Evaluation of user-friendliness

If possible, SKUP evaluations are carried out using three lot numbers of test strips from separate and time-spread productions. In at least one of the PHCCs, the evaluators should not be biomedical laboratory scientists (BLSs).

SKUP offers various kinds of evaluations, but in principle, the end-users should always participate. If the part performed by the intended users is not included, the report code is followed by an asterisk (*), indicating a special evaluation. Only evaluations where the end-users are involved will fully demonstrate the quality of the product. This evaluation of Xprecia Stride was performed both under optimal conditions and by the intended users.

4. Quality goals

4.1. Analytical quality

At present, there are no generally recognised analytical quality goals for the determination of prothrombin time International Normalized Ratio, PT (INR), and no international standard for evaluation of Point of Care test instruments for PT (INR) in primary health care.

The International Organization for Standardization (ISO) 17593 standard [2] gives requirements for accuracy for self-testing systems of oral anticoagulant therapy. There is no performance criterion for imprecision in the standard. In SKUP's opinion, the quality goals for accuracy in the standard, ±30% for 90% of the PT (INR) results in the therapeutic range 2 – 4,5 INR, is too tolerant.

Setting quality goals based on biological variation is an acknowledged method [3,4]. It is recommended that analytical imprecision (repeatability, analytical coefficient of variation; CV_A) should be less than, or equal to, half the intra-individual biological variation. For systems used for monitoring, the analytical performance should aim at low imprecision compared to the within-subject biological variation. Ricos *et al*. [5] state the intra-individual biological variation for prothrombin time to 4%. According to Kjeldsen *et al.* [6], the "in-treatment within-subject biological variation" of PT (INR) is 10,1%. Van den Besselar *et al*. [7] recommend a CV_A ≤4,5%, while Lassen *et al.* [8] recommend a CV_A ≤4,7%.

For PT (INR) measurements in primary health care in Norway, Trydal *et al*. [9] recommend a CV ≤5% in the therapeutic range and a minimum of 95% of the results within ±20% compared with the hospital method. A committee appointed by the National Ministry of Health in Denmark has specified the requirements of analytical quality for PT (INR) for instruments used in primary health care [10,11] with an imprecision ≤5% and a bias ≤6%.

SKUP recommends that PT (INR) devices used in primary health care should achieve a repeatability CV ≤5,0%. SKUP has not set a separate goal for bias, but a bias of 5% is used to calculate a quality goal for allowable deviation according to the model below. In all method evaluations and comparisons, the imprecision of the comparison method must also be taken into account. SKUP allows an imprecision of the comparison method up to 3%. In addition, SKUP has estimated the contribution of inter-laboratory-variation to 3% and the contribution of a probable matrix effect to 5% to account for sample specific errors when comparing two different methods (Quick and Owren).

$$\text{Allowable deviation} = |\pm\text{bias}| + 1{,}65 \times \sqrt{CV^2_{\text{test method}} + CV^2_{\text{comparison method}} + CV^2_{\text{between lab}} + CV^2_{\text{matrix}}}$$

$$= 5 + 1{,}65 \times \sqrt{25 + 9 + 9 + 25} = 5 + 13{,}6 = \pm 18{,}6\% \approx \pm 20\%$$

4.2. User-friendliness

The evaluation of user-friendliness is carried out by asking the evaluating persons to fill in a questionnaire divided into four subareas, see section 6.5.

Technical errors

SKUP recommends that the fraction of tests wasted caused by technical errors should not exceed 2%.

4.3. Principles for the assessments

To qualify for an overall good assessment in a SKUP evaluation, the measuring system must show satisfactory analytical quality as well as satisfactory user-friendliness.

4.3.1. Assessment of the analytical quality

The analytical results are assessed according to pre-set quality goals.

Precision

The decision whether the achieved coefficient of variation (CV) fulfils the quality goal or not, is made on a 5% significance level. The distinction between the ratings, and the assessment of precision according to the quality goal, are shown in table 1.

Table 1. The rating of precision

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

Trueness

SKUP does not set separate quality goals for bias. The bias will be discussed as part of the total measuring error illustrated in a difference plot. The confidence interval (CI) of the measured bias is used for deciding if a difference between the two methods is statistically significant (two-tailed test, 5% significance level). The term trueness is related to the results achieved under optimal conditions. Proven systematic deviation of the results achieved by the intended users, will be discussed in relation to the bias found under optimal conditions.

Accuracy

The accuracy is illustrated in a difference plot with limits for the allowable deviation according to the quality goal. The fraction of results within the limits is counted. The accuracy is assessed as either fulfilling the quality goal or not fulfilling the quality goal.

Bias with three lots of test strips
Separate lot calculations are not performed. The results achieved with the three lots are included in the assessment of accuracy in the difference plot for the results achieved under optimal conditions. If distinct differences between the lots appear, this will be pointed out and discussed.

4.3.2. Assessment of the user-friendliness

The user-friendliness is assessed according to the answers and comments given in the questionnaire (see section 6.5). For each question, the evaluator can choose between three given ratings. The responses from the evaluators are reviewed and summed up. To achieve the overall rating "satisfactory", the tested equipment must reach the total rating of "satisfactory" in all four subareas of characteristics described in section 6.5.

Technical errors
The evaluating person registers error codes, technical errors and failed measurements during the evaluation. The fraction of tests wasted caused by technical errors is calculated and taken into account in connection with the assessment of the user-friendliness.

4.4. SKUP´s quality goals in this evaluation

As agreed upon when working on the protocol, the results from the evaluation of Xprecia Stride are assessed against the following quality goals:

Repeatability (CV) ..... ≤5,0%

Allowable deviation
in the individual result from the comparison method result..... ≤±20%

Required percentage of individual results
within the allowable deviations* ..... ≥95%

User-friendliness, overall rating..... Satisfactory

*If more than 1% of the results deviate more than ±25%, this will be pointed out and discussed.

5. Materials and methods

5.1. Definition of the measurand

The Committee on Nomenclature, Properties and Units (C-NPU) describes clinical laboratory tests in a database [12]. In the NPU-database the specifications for the measurand in this evaluation are as shown in table 2.

Table 2. NPU-specifications

NPU code	Name of test according to NPU	Unit
NPU01685	P—Coagulation, tissue factor-induced; relative time(actual/normal; INR; IRP 67/40; proc.)	–
NPU21717	P—Coagulation, tissue factor-induced; rel.time(actual/norm; INR; IRP 67/40; II+V+VII+X)	–

The analytical test according to NPU01685 refers to measurements performed with the Owren method. The test is mainly determined by the concentration of the Vitamin K dependent coagulation factors II, VII and X. The analytical test according to NPU21717 refers to measurements performed with the Quick method. The test is mainly determined by the concentration of the Vitamin K dependent coagulation factors, in addition to fibrinogen (factor I) and factor V.

In this evaluation, the comparison method is an Owren method traceable to WHO IRP 67/40, through RBT/90 [13-15] while the evaluated method, Xprecia Stride, is a modified Quick method traceable to WHO IRP 67/40, through rTF/09. Even if the tests according to NPU01685 and NPU21717 are not measuring exactly the same plasma components, the results are traceable to the same reference preparation, IRP 67/40, and the test results are used as if they are comparable. The term “PT (INR)” will be used for the measurand in this report. As the measurement result is a ratio of the actual coagulation time divided with the normal coagulation time, there is no unit.

5.2. The evaluated measurement system Xprecia Stride

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

The Xprecia Stride Coagulation system is intended for the determination of PT (INR). Xprecia Stride™ Coagulation System includes:

- Xprecia Stride Coagulation Analyzer (figure 1)
- Xprecia™ Systems PT (INR) Strips
- Xprecia™ Systems PT Controls

The product is intended for multiple-patient use by professional healthcare providers in the management of patients treated with warfarin, an oral vitamin K antagonist. The system uses fresh whole blood capillary samples.

Figure 1. Xprecia Stride Analyzer

The Xprecia Systems PT (INR) Strip is a single-use electrochemical cell. It contains the reagent Dade® Innovin®, which is a preparation of purified recombinant human tissue factor combined with synthetic phospholipids, calcium and stabilisers. A sample chamber in the test strip is filled with the blood sample by capillary action. Contact with blood dissolves the reagents, which initiates clotting, producing thrombin in the process. Thrombin cleaves an electroactive group from a synthetic peptide, i.e. fibrinogen is not involved. This can be detected at the electrodes by putting a voltage across the electrodes. Xprecia Stride measures the electrical current produced to provide the PT (INR). The Xprecia System is sensitive to the coagulation factors II, V, VII and X.

A barcode on the strip vial contains the batch calibration information. The Xprecia Stride Analyzer stores at least two vial calibration information sets. Each test strip has to be scanned prior to use. Upon the start of a test, the analyzer checks that the calibration information from the vial correlates with the information from the strip.

Internal analytical quality controls: The manufacturer produces the control kit Xprecia™ Systems PT Controls with PT Control 1 in the normal range and PT Control 2 in the therapeutic range. The material is lyophilised human plasma to be reconstituted with $CaCl_2$ diluent.

For technical details about Xprecia Stride, see table 3. For more information about the Xprecia Stride system, name of the manufacturer and the suppliers in the Scandinavian countries, see attachment 2 and 3. For product specifications in this evaluation, see attachment 4.

Table 3. Technical details from the manufacturer

Technical details for Xprecia Stride	
Sample material	Fresh capillary blood
Sample volume	6 µl
Measuring time	<1,6 minutes (depending on INR-level)
Measuring range	0,8 – 8,0 INR
Haematocrit	25% – 55%
Storage capacity	640 patient test results
Electrical power supply	Disposable alkaline batteries/ Rechargeable nickel batteries

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 this evaluation

The selected comparison method in this evaluation is the routine method for PT (INR) in the laboratory of Haraldsplass Deaconess Hospital, hereafter called "the comparison method".

The method is accredited after NS-EN ISO 15189 (2012) (Norsk Standard_Europeisk Norm International Organization for Standardization.

Instrument:	STA-R Evolution, STAGO	
Reagent:	STA-SPA+, Diagnostica STAGO Prothrombincomplex Assay	
Principle:	Owren's method, rabbit brain thromboplastin (RBT) and adsorbed bovine plasma	
Traceability:	World Health Organization's (WHO's) manual tilt tube technique and the reference thromboplastin WHO IRP 67/40, through RBT/90 [13-15]	
Calibrators:	Two point's calibration with PT (INR)-calibrators from Equalis (External quality assessment for clinical laboratory investigations in Sweden)	
Reference interval	0,9 – 1,2 INR	
Therapeutic range	venous indication	2,0 – 3,0 INR
	arterial indication	2,5 – 3,5 INR

Internal analytical quality control

Internal analytical quality control samples, two levels (STA-Scandinorm PT (INR) and STA-Scandipath PT (INR), STAGO), were measured each evaluation day on the comparison method. The reproducibility (CV), as achieved with the quality control material of the comparison method, was calculated.

External analytical quality control

The hospital laboratory participates in Noklus/NKK (Norwegian Quality Improvement of Primary Care Laboratories/Norwegian Clinical Chemistry EQA Program) external quality assessment (EQA) scheme for PT (INR) with two levels four rounds per year. The materials are freshly frozen pooled citrate plasma from Norwegian donors. The assigned values for PT (INR) are based on consensus values from participants using PT (INR)-calibrators from Equalis.

5.3.2. Verification of the analytical quality of the comparison method

Precision

The repeatability (CV) of the comparison method was calculated from duplicate measurements of venous citrate samples from the patients participating under optimal conditions. The laboratory´s given limit for the imprecision of the comparison method was 4,0% at level 1,0 – 3,4 INR.

Trueness
The Norwegian and Swedish hospital laboratories use PT (INR) calibrators from Equalis. In Denmark, the hospital laboratories use PT (INR) calibrators from the Danish Institute of External Quality Assurance for Laboratories in Health Care (DEKS). The calibrating systems from Equalis and DEKS are different with respect to the production of the materials as well as to the way the PT (INR) target values are assigned.

- PT (INR) calibrators from Equalis were analysed as samples on the comparison method on different occasions during the evaluation. The calibrator material is a pool of citrated anti-coagulated freeze-dried plasma of human origin (Swedish donors). The certified values are traceable to an internationally agreed reference measurement procedure (WHO's manual tilt tube technique) and the reference thromboplastin WHO IRP 67/40, through RBT/90 [13-15]. The procedures used to assign values are described in several publications and documents [16-18].

- PT (INR) calibrators from DEKS were analysed as samples on the comparison method at the start, in the middle and in the end of the evaluation to get a link to the Danish PT (INR) level. The calibration materials from DEKS are freshly frozen pooled citrate-plasmas, which serve as national reference plasmas in Denmark. The DEKS calibration is a three point's calibration with a normal, therapeutic and high PT (INR). The assigned values come from three Nordic expert laboratories.

- On one occasion in the evaluation period, PT (INR) controls from Noklus were analysed on the comparison method.

5.4. The evaluation

5.4.1. Planning of the evaluation

Inquiry about an evaluation
Siemens Healthcare Diagnostics AS via Country Business Manager/ Point-of-Care & Channel Manager Thor Hæstad applied to SKUP in April 2015 for an evaluation of Xprecia Stride.

Protocol, arrangements and contract
In November 2015, the protocol for the evaluation was approved, and Siemens Healthcare Diagnostics AS and SKUP signed a contract for the evaluation. BLSs at SKUP were assigned to do the practical work with Xprecia Stride in the evaluation under optimal conditions. Two primary health care centres, Danmarksplass Legesenter and Helse+ Gården senter from Hordaland county, agreed to represent the intended users in this evaluation.

Training
Thor Hæstad from Siemens Healthcare Diagnostics AS demonstrated the Xprecia Stride system for SKUP and the two PHCCs. The training in the PHCCs reflected the training usually given to the intended users. The requesting company was not allowed to contact or supervise the evaluators during the evaluation period.

5.4.2. Evaluation sites and persons involved

The practical work was carried out during 13 weeks under optimal conditions at Noklus and 14 weeks in the PHCCs, ending in March 2016. At Noklus four BLSs were involved in the practical work. The hospital laboratory serving the comparison method, has approximately 20 employees. Haraldsplass Deaconess Hospital is a university hospital. PHCC1 has five physicians. From PHCC1 three health secretaries and one medical secretary participated in the evaluation. They use capillary blood samples in their routine method for measurements of PT (INR). PHCC2 has four physicians. From PHCC2 four health secretaries and one nurse participated. They use capillary blood samples in their routine method for measurements of PT (INR).

5.4.3. The evaluation procedure under optimal conditions

Internal analytical quality control

Internal analytical quality control samples for Xprecia Stride, two levels (PT Control 1 and PT Control 2, Siemens Healthcare Diagnostics INC), were measured each evaluation day on Xprecia Stride.

Recruitment of patients

Patients were recruited both by announcement in media and in primary health care centres. The patients were asked if they were willing to donate two capillary and one venous blood sample for the evaluation. Participation was voluntary and verbal consent was considered sufficient based on national regulations. Blood samples were collected from patients who had been stable on vitamin K antagonist treatment for a minimum of 4 weeks. Patients with known Lupus were not included.

Handling of the samples and measurements

Fresh whole blood capillary samples were measured in duplicate (two fingersticks per patient) on Xprecia Stride. The puncture site was disinfected with alcohol pads and the area dried completely before sampling. Disposable lancing devices with depth settings 1,8 mm were used. The first drop of capillary blood was applied to the test strip immediately, in accordance with the instructions from the manufacturer. If the blood smeared or run, it was wiped off with a clean dry tissue/gauze and the second blood drop was used. Three lot numbers of Xprecia Stride test strips were used at each site during the course of the evaluation. In case of error codes, the test was repeated if possible until a result was obtained.

Samples for the comparison method were obtained from venous puncture and collected into vacutainer tubes with 3,2% sodium citrate. The venous samples were taken immediately before the measurements on Xprecia Stride. The tubes were inverted 3 – 4 times to ensure thorough mixing and kept at room temperature until transported to the hospital laboratory later the same day. In the laboratory the samples were centrifuged for 15 minutes at 2000 g. The citrate plasma was measured in duplicate on the comparison method within eight hours from sampling.

5.4.4. The evaluation procedure for the intended users

Internal analytical quality control

Internal analytical quality control samples for Xprecia Stride (PT Control 1 and PT Control 2, Siemens Healthcare Diagnostics INC) were measured each evaluation day on Xprecia Stride, one level per day alternating between the two levels.

Recruitment of patients
Patients coming into primary health care centres for PT (INR) measurements, were asked if they were willing to donate two capillary and one venous blood sample extra for the evaluation. Participation was voluntary and verbal consent was considered sufficient based on national regulations. Blood samples were collected from patients who had been stable on vitamin K antagonist treatment for a minimum of 4 weeks. Patients with known Lupus were not included.

Handling of the samples and measurements
Fresh whole blood capillary samples were measured in duplicate (two fingerstick per patient) on Xprecia Stride. The puncture site was disinfected with alcohol pads and the area dried completely before sampling. Disposable lancing devices with depth settings 1,8 mm were used. The first drop of capillary blood was applied to the test strip immediately after sampling, in accordance with the instructions from the manufacturer. If the blood smeared or runned, it was wiped off with a clean dry tissue/gauze and the second blood drop was used. Three lot numbers of Xprecia Stride test strips were used at each site during the course of the evaluation. In case of error codes, the test was repeated if possible until a result was obtained

Samples for the comparison method were obtained from venous puncture and collected into 2,7 mL vacutainer tubes with 3,2% sodium citrate. The venous samples were taken immediately before the measurements on Xprecia Stride. The tubes were inverted 3 – 4 times to ensure thorough mixing and kept at room temperature until transported to the hospital laboratory later the same day. In the laboratory the samples were centrifuged for 15 minutes at 2000 g. The protocol stated that the citrate plasma had to be analyzed in duplicate for PT (INR) on the comparison method within 48 hours after sampling. This is in accordance with the procedures for the comparison method. In practice, all but two of the PT (INR) measurements from the PHCCs were completed within 24 hours.

6. Results and discussion

Statistical expressions and calculations used by SKUP are shown in attachment 5.

6.1. Number of samples

Scheduled number of samples in this evaluation was 100 patient samples measured in duplicate under optimal conditions and 80 patient samples measured in duplicate by the intended users. Under optimal conditions, 101 patients were recruited (SKUP ID 1-101). In the evaluation performed by the intended users, PHCC1 and PHCC2 recruited 40 patients each (SKUP ID 111-150 and SKUP ID 201-240). The results from the comparison method covered the interval 1,0 – 4,3 INR. One individual (SKUP ID 85) was not on warfarin therapy. Most of the results were within the interval 2,0 – 3,5 INR, therefore the results achieved in the hospital laboratory were divided into two, instead of three PT (INR) levels. This also provides an easier comparison with the results achieved in the two PHCCs, were the results are divided into two levels because of the lower number of results. An account of the number of samples not included in the calculations, is given below.

Missing results

- From PHCC1 and PHCC2 an internal analytical quality control result from one day each was missing. The results from the patient samples this day were still included in the calculations.
- Under optimal conditions, internal analytical quality control results from one day were missing. The results from the patient samples this day were still included in the calculations.
- ID 237; there is no results from the comparison method as the venous sample never arrived the hospital laboratory. The results from Xprecia Stride were included in the calculation of repeatability.

Omitted results

- ID 206 and 210; same patient was included twice. The ID number 210 was assigned at the second visit. The results from this patient were systematic below the limits for allowable deviation from the comparison method on both occasions, which indicates an individual sample matrix effect. To avoid sample matrix contribution twice from one individual, the results from SKUP ID 210 were excluded from all calculations.

Excluded results

Statistical outliers in SKUP evaluations are detected by the criterion promoted by Burnett [19].

- ID 11; the results from the comparison method were classified as outliers according to Burnetts's model in the calculation of repeatability. The results were not included in any calculations besides the calculation of repeatibility were the results are from Xprecia Stride only.
- ID 14 and ID 224; the results from Xprecia Stride were classified as outliers according to Burnetts's model in the calculation of repeatability. The results were removed before calculation of trueness, but were included in the assessment of accuracy (the first of the duplicate measurements).
- ID 37 and ID 132; the results from Xprecia Stride were classified as outliers according to Burnett's model in the calculation of trueness. The results were included in the assessment of repeatability and accuracy (the first of the duplicate measurements).

Recorded error codes, technical errors and failed measurements
Under optimal conditions, the following error messages were reported on Xprecia Stride:
- 1 x 02-02; Used test strip inserted (the test strip was bent in the end)
- 1 x 04-09; Test strip fill error (double-filled the sample area)
- 5 x 04-10; Test strip fill error (did not fill the sample area completely)

Handled by the intended users, the following error messages were reported on Xprecia Stride:
- 2 x 04-09; Test strip fill error (double-filled the sample area)
- 12 x 04-10; Test strip fill error (did not fill the sample area completely)

Most of the error messages were related to the handling of the sample, in total (20/360)x100 = 5,6% error messages. The error message 02-02, was interpreted as a technical error and led to wasted test strip. The fraction of tests wasted due to technical errors was estimated to (1/360)x100 = 0,3%.

The SKUP recommendation of a fraction of ≤2% tests wasted caused by technical errors was achieved.

6.2. Analytical quality of the selected comparison method

6.2.1. Internal analytical quality control
All results from the internal analytical quality control, two levels (STA-Scandinorm and STA-Scandipath PT (INR)), were within the allowable control limits (data not shown). The reproducibility achieved with the internal analytical quality control samples was approximately 1,6% for level 1 (n=376) and 2,2% for level 2 (n=375).

6.2.2. The precision of the comparison method
Duplicate measurements of each venous citrate patient sample were performed on the comparison method. The results were checked to meet the imposed condition for using formula 1 in attachment 5. 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 4. The results are sorted and divided into two levels according to the mean of the results of the comparison method. Raw data is attached for the requesting company only, attachment 6.

Table 4. Repeatability, PT (INR), venous citrate samples, comparison method

PT (INR) level, Comparison method	n	Excluded results	Mean value (interval), PT (INR)	CV (90% CI), %
<2,5	61	0	2,1 (1,01 – 2,48)	0,8 (0,5 – 1,0)
≥2,5	40	1*	2,9 (2,52 – 4,15)	0,8 (0,7 – 1,0)

*The given numbers of results (n) were counted before the exclusion of results. Mean and CV were calculated after the exclusion of results. ID 11 is a statistical outlier according to Burnett's model [19] and therefore excluded. An account of the number of samples is given in section 6.1.

Discussion
The CV for the comparison method was 0,8%. This is well below the laboratory´s given limit for the imprecision (4,0%) of the comparison method.

6.2.3. The trueness of the comparison method

To demonstrate the trueness of the comparison method, calibrators from Equalis were analysed as samples halfway (lot 28, 29 and 30) and at the end (lot 31, 32 and 33) of the evaluation. The calibrators from DEKS were analysed on three different occasions; at start-up, halfway and at the end of the evaluation. The results achieved with the Equalis calibrators are shown in table 5. The results achieved with DEKS calibrators are shown in table 6.

Table 5. Equalis PT (INR) calibrators measured on the comparison method

Material		Assigned value, PT (INR) (uncertainty)	Date	n	Mean value, PT (INR) STA-R
Equalis INR calibrator Low	lot 28 and 31	**1,05** (0,96 – 1,14)	12.01.16	5	1,06
			03.03.16	5	1,05
Equalis INR calibrator High	lot 29	**3,14** (2,57 – 3,71)	12.01.16	5	3,19
	lot 32	**2,82** (2,56 – 3,08)	03.03.16	5	2,95
Equalis INR control	lot 30	**2,48** (2,09 – 2,87)	12.01.16	5	2,48
	lot 33	**2,30** (2,09 – 2,51)	03.03.16	5	2,31

Table 6. DEKS PT (INR) calibrators measured on the comparison method

Material	Assigned value, PT (INR) (uncertainty)	Date	n	Mean value, PT (INR) STA-R
DEKS INR calibrator Normal	**1,00** (0,98 – 1,03)	04.12.15	5	0,98
		12.01.16	5	1,01
		03.03.16	5	0,99
DEKS INR calibrator Therapeutic	**2,26** (2,19 – 2,33)	04.12.15	5	2,16
		12.01.16	5	2,25
		03.03.16	5	2,17
DEKS INR calibrator High	**3,74** (3,59 – 3,89)	04.12.15	5	3,33
		12.01.16	5	3,52
		03.03.16	5	3,37

Results achieved for external quality control material from the Noklus/NKK EQA-scheme in August and December 2015, and February 2016 show that the laboratory's deviations from the assigned value in the three surveys were (- 0,05), (- 0,02), (-0,03) INR at a normal level and

(-0,08), (-0,14), (-0,10) INR at a therapeutic level. Results of the Noklus/NKK control material, which were also analysed on one occasion during the evaluation, were within the acceptable limits for the control material (data not shown).

Discussion
The results from the comparison method were in agreement with the Equalis calibrators. The results from the EQA-scheme also showed that the comparison method was in agreement with the other hospital laboratories (n=62−66) using PT (INR) calibrators from Equalis. The comparison method tended to be approximately 0,1 INR lower than the assigned values in the therapeutic PT (INR) level for both the Noklus controls and DEKS calibrators, and approximately 0,3 INR lower than the assigned value in the high PT (INR) level for the DEKS calibrator.

6.3. Analytical quality of Xprecia Stride under optimal conditions

The results below reflect the analytical quality of Xprecia Stride under optimal conditions. The results documents the quality of the system under conditions as favourable as possible for achieving good analytical quality.

6.3.1. Internal analytical quality control

All results from the internal analytical quality control, two levels (PT Control 1 and PT Control 2), were within the allowable control limits (data not shown). Internal analytical quality control results from one day were missing, as described in section 6.1. The reproducibility achieved with the internal analytical quality control samples were 3,8% for level 1 (n=31) and 5,1% (n=20) and 5,6% for level 2 (n=11), two different lot numbers respectively. Raw data is attached for the requesting company only, attachment 7.

6.3.2. The precision of Xprecia Stride

Two capillary samples from each patient were measured on Xprecia Stride. The results were checked to meet the imposed condition for using formula 1 in attachment 5. 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 are sorted and divided into two levels according to the mean of the results of Xprecia Stride. Raw data is attached for the requesting company only, attachment 8.

Table 7. Repeatability, PT (INR), capillary samples, Xprecia Stride. Results achieved under optimal conditions.

PT (INR) level, Xprecia Stride	n	Excluded results	Mean value (interval), PT (INR)	CV (90% CI), %
<2,5	68	0	2,0 (1,00 – 2,45)	4,7 (4,0 – 5,5)
≥2,5	33	1*	3,1 (2,50 – 4,45)	5,3 (4,5 – 6,2)

*The given numbers of results (n) are counted before the exclusion of results. Mean and CV are calculated after the exclusion of results. ID 14 is statistical outlier according to Burnett's model [19] and therefore excluded. An account of the number of samples is given in section 6.1.

Discussion
At PT (INR) level <2,5 the CV achieved under optimal conditions was 4,7%. As the upper CI value is above 5,0%, the CV is not statistically significant below the quality goal. At PT (INR) level ≥2,5 the CV was 5,3%. This is higher than the quality goal, but not statistically significant higher.

Conclusion
Under optimal conditions the quality goal for repeatability (CV≤5,0%) was most likely fulfilled at PT (INR) level <2,5. At PT (INR) level ≥2,5 the quality goal was most likely not fulfilled.

6.3.3. The trueness of Xprecia Stride

The mean deviation (bias) of Xprecia Stride results from the comparison method was calculated. The bias is presented with a 95% CI in table 8. The results are sorted and divided into two levels according to the mean results of the comparison method. Raw data is attached for the requesting company only, attachment 6 and 8.

Table 8. Bias, PT (INR), capillary samples, Xprecia Stride. Results achieved under optimal conditions.

PT (INR) level, Comparison method	n	Excluded results	Mean value Comparison method, PT (INR)	Mean value Xprecia Stride, PT (INR)	Bias (95% CI), PT (INR)	Bias, %
<2,5	61	1*	2,1	2,0	-0,09 ((-0,13) – (-0,05))	-4,4
≥2,5	40	2*	3,0	2,9	-0,03 ((-0,15) – (+0,08))	-1,1

*The given numbers of results (n) are counted before the exclusion of results. Mean and bias are calculated after the exclusion of results. ID 11, ID 14 and ID 37 are statistical outliers according to Burnett's model [19] and therefore excluded. An account of the number of samples is given in section 6.1.

Discussion
For PT (INR) level <2,5 a small, but statistically significant bias was shown. The Xprecia Stride system gave results 4,4% lower than the comparison method with a bias of -0,09 INR. For PT (INR) level ≥2,5 no significant bias was pointed out.

6.3.4. The accuracy of Xprecia Stride

To evaluate the accuracy of PT (INR) results on Xprecia Stride, the agreement between Xprecia Stride and the comparison method is illustrated in a difference plot (figure 2). The limits for the allowable deviation according to the quality goal (±20%), are shown with stippled lines.
All the first measurements from Xprecia Stride are included in the plot. The plot illustrates both random and systematic errors, reflecting the total measuring error in the Xprecia Stride results. Raw data is attached for the requesting company only, attachment 6 and 8.

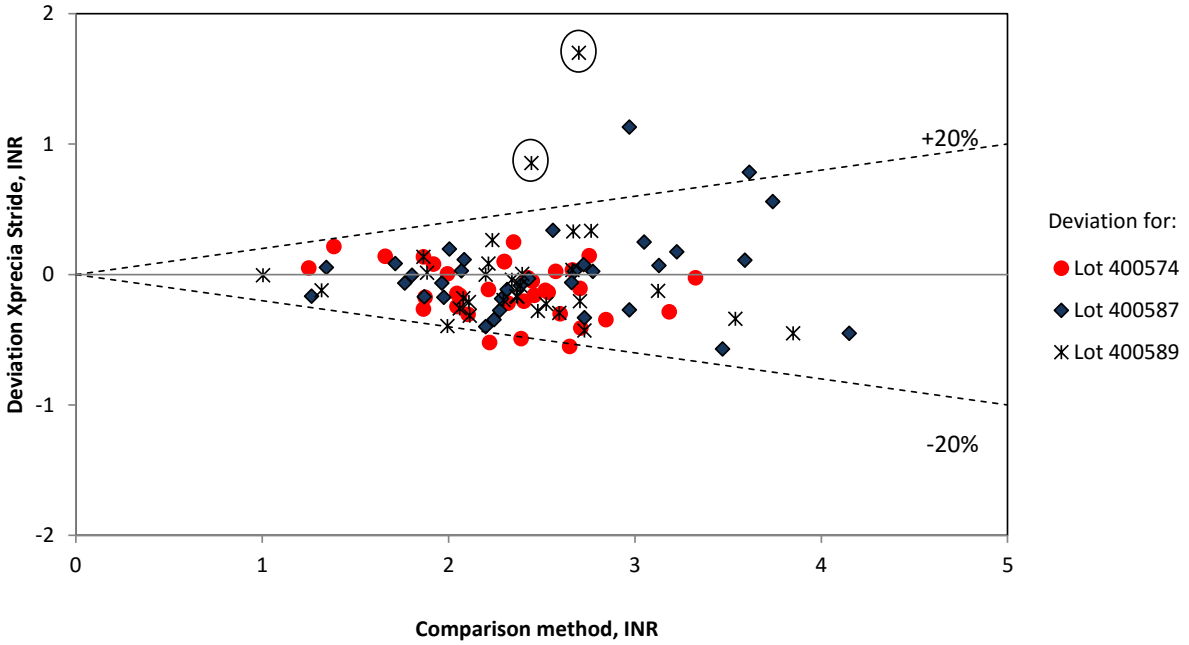

Figure 2. Accuracy of PT (INR) on Xprecia Stride under optimal conditions. The x-axis represents the mean PT (INR) result of the comparison method. The y-axis represents the PT (INR) deviation in INR of the first capillary sample measurement on Xprecia Stride from the mean result of the corresponding sample of the comparison method. The different lots of test strips are illustrated as lot 400574 (●), lot 400587 (♦) and lot 400589 (x). Stippled lines represent allowable deviation limits of ±20%. Number of results (n) = 100. ID 14 and ID 37, statistical outliers from the calculations of repeatability and bias respectively, are illustrated with a circle around the symbol. An account of the number of samples is given in section 6.1.

Discussion

Figure 2 shows a tendency of more results below zero than above, which correspond to the small negative calculated bias in 6.3.3. Seven of 100 results achieved under optimal conditions were outside the allowable deviation limits of ±20%, i.e. 93% were inside the limits. According to the quality goal, at least 95% of the results should be within the limits ±20%.

Three of the results were more than 25% higher than the comparison method. There was no error message from Xprecia Stride or other comments for the result with the highest deviation (deviation 1,7 INR), but in the calculation of repeatability the result was classified as an outlier according to Burnett's model [19]. For the result classified as an outlier in the calculation of trueness (deviation 0,86 INR) the duplicate measurements gave reproducible values. A reproducible deviation like this can occur as a result of sample matrix effect, i.e. components in the sample affecting the two methods differently. The sensitivity of the Quick- and Owren method for various coagulation factors is different. The differences in the reagents can additionally be amplified due to different dilution of the samples. The Owren method has a 1:21 dilution of the samples whereas the blood is undiluted in the modified Quick method (blood applied directly onto the dry reagent strip). Greater or lesser degree of sample dilution could be an important contributor to systematic PT (INR)-discrepancies in individual patients. One should always be aware of the possibility for such deviating results when comparing Quick- and Owren-based methods. For this particular patient further investigation for Lupus was initiated.

Conclusion

Under optimal conditions the quality goal for accuracy was not fulfilled.

6.3.5. Bias with three lots of test-strips

No distinct differences between the three lots were observed. Separate lot calculations were not performed.

6.4. Analytical quality of Xprecia Stride achieved by intended users

The results below reflect the analytical quality of Xprecia Stride under real-life conditions in the hands of the intended users. The results may deviate from the results achieved under optimal conditions.

6.4.1. Internal analytical quality control

All results from the internal analytical quality control, two levels (PT Control 1 and PT Control 2), were within the allowable control limits (data not shown). An internal analytical quality control result from one day each was missing in PHCC1 and PHCC2, as described in section 6.1 The reproducibility achieved with the internal analytical quality control samples from both PHCC1 and PHCC2 were 4,5% for level 1 (n=20) and 3,6% for level 2 (n=15). Raw data is attached for the requesting company only, attachment 9.

6.4.2. The precision of Xprecia Stride

Two capillary samples from each patient were measured on Xprecia Stride. The results were checked to meet the imposed condition for using formula 1 in attachment 5. 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 9. The results are sorted and divided into two levels according to the mean of the results of Xprecia Stride. Raw data is attached for the requesting company only, attachment 10.

Table 9. Repeatability, PT (INR), capillary samples, Xprecia Stride. Results achieved by intended users.

PT (INR) level, Xprecia Stride	n	Excluded results	Mean value (interval), PT (INR)	CV (90% CI), %
PHCC1				
<2,5	29	0	1,9 (1,10 – 2,40)	4,5 (3,7 – 5,8)
≥2,5	11	0	3,0 (2,50 – 4,00)	7,1 (5,3 – 11,2)
PHCC2				
<2,5	24	0	2,0 (1,45 – 2,40)	5,5 (4,6 – 7,1)
≥2,5	15	1*	2,9 (2,50 – 3,60)	6,4 (4,8 – 9,6)

*The given numbers of results (n) are counted before the exclusion of results. Mean and CV are calculated after the exclusion of results. ID 224 is statistical outlier according to Burnett's model [19] and therefore excluded. An account of the number of samples is given in section 6.1.

Discussion

At PT (INR) level <2,5 the CV achieved by the intended users was 4,5% and 5,5% in PHCC1 and PHCC2, respectively. As both the CIs include 5,0%, the CVs are not statistically significant

below (PHCC1) or above (PHCC2) the quality goal. At PT (INR) level ≥2,5 the CV was 7,1% and 6,4%. This is higher than the quality goal, but for PHCC2 not statistically significant higher.

Conclusion
The quality goal for repeatability (CV≤5,0%) was most likely fulfilled in PHCC1 at PT (INR) level <2,5. In PHCC2, the quality goal was most likely not fulfilled at this level. At PT (INR) level ≥2,5 the quality goal for repeatability was not fulfilled in PHCC1 and most likely not fulfilled in PHCC2. In total, the quality goal for repeatability was not fulfilled under real-life conditions.

6.4.3. The bias of Xprecia Stride

The mean deviation (bias) of Xprecia Stride results from the comparison method was calculated. The bias is presented with a 95% CI in table 10. The results are sorted and divided into two levels according to the mean results of the comparison method. Raw data is attached for the requesting company only, attachment 6 and 10.

Table 10. Bias, PT (INR), capillary samples, Xprecia Stride. Results achieved by intended users.

PT (INR) level, Comparison method	n	Excluded results	Mean value Comparison method, PT (INR)	Mean value Xprecia Stride, PT (INR)	Bias (95% CI), PT (INR)	Bias, %
PHCC1						
<2,5	26	1*	1,9	1,8	-0,11 ((-0,16) – (-0,05))	-5,5
≥2,5	14	0	3,0	2,9	-0,12 ((-0,29) – (+0,04))	-4,3
PHCC2						
<2,5	19	0	2,1	1,9	-0,17 ((-0,25) – (-0,09))	-8,3
≥2,5	19	1*	3,0	2,7	-0,23 ((-0,37) – (-0,09))	-8,2

*The given numbers of results (n) are counted before the exclusion of results. Mean and bias are calculated after the exclusion of results. ID 132 and ID 224 are statistical outliers according to Burnett's model [19] and therefore excluded. An account of the number of samples is given in section 6.1.

Discussion
For PT (INR) level <2,5 a statistically significant bias was shown for the results from both PHCC1 and PHCC2. Xprecia Stride gave results between 0,11 – 0,17 INR lower than the comparison method. For PT (INR) level ≥2,5 no significant bias was pointed out in PHCC1, but in PHCC2 Xprecia Stride gave results 8,2% lower than the comparison method. The bias for this level in PHCC2 was -0,23 INR.

6.4.4. The accuracy of Xprecia Stride

To evaluate the accuracy of PT (INR) results on Xprecia Stride, the agreement between Xprecia Stride and the comparison method is illustrated in a difference plot (figure 3). The limits for the allowable deviation according to the quality goal (±20%), are shown with stippled lines. All the first measurements from Xprecia Stride are included in the plot. The plot illustrates both random and systematic errors, reflecting the total measuring error in the Xprecia Stride results. Raw data is attached for the requesting company only, attachment 6 and 10.

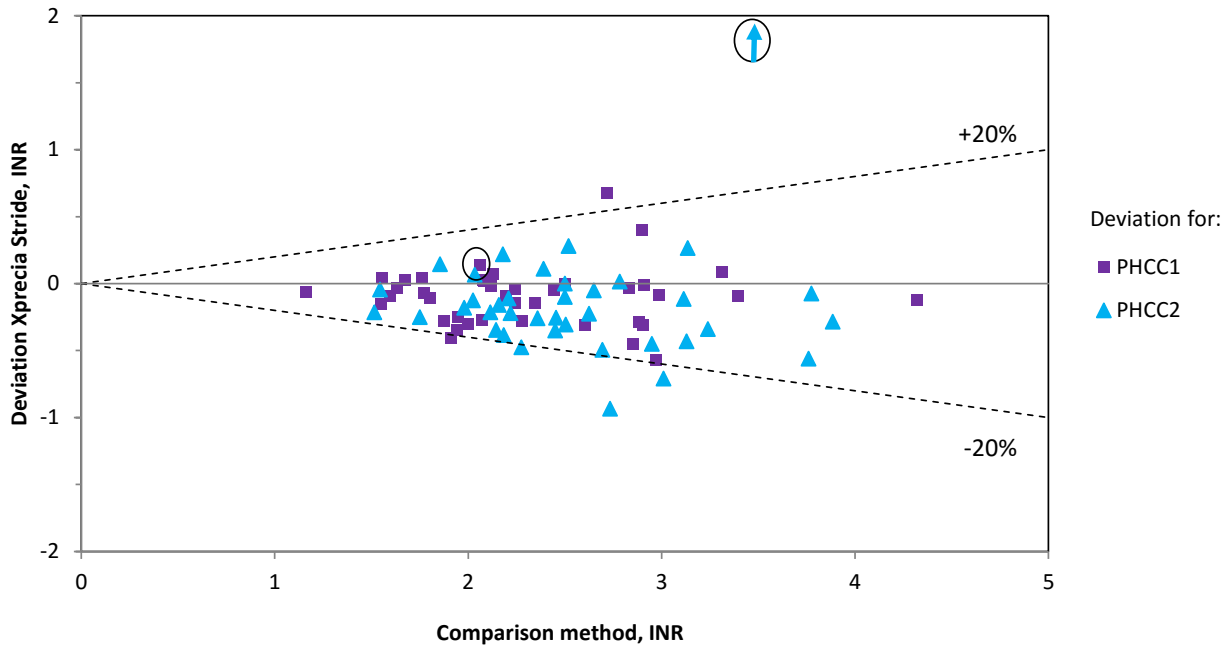

Figure 3. Accuracy of PT (INR) on Xprecia Stride achieved by intended users. The x-axis represents the mean PT (INR) result of the comparison method. The y-axis represents the PT (INR) deviation in INR of the first capillary sample measurement on Xprecia Stride from the mean result of the corresponding sample of the comparison method. The results from PHCC1 are represented with the symbol (■) and results from PHCC2 with the symbol (▲). Stippled lines represent allowable deviation limits of ±20%. Number of results (n) = 78. ID 224 and ID 132, statistical outliers from the calculations of repeatability and bias, respectively, are illustrated with a circle around the symbol. ID 224 is marked with an arrow as the result is outside the plot. An account of the number of samples is given in section 6.1.

Discussion

Figure 3 shows a more distinct tendency of results below zero than above, compared to the results achieved under optimal conditions, 6.3.4. This correspond to the calculated negative biases in 6.4.3. Six of 78 results achieved by the intended users were outside the allowable deviation limits of ±20%, i.e. 92% were inside the limits.

Two of the results deviated more than ±25% from the comparison method. The result with deviation +2,2 INR was classified as an outlier according to Burnett's model in the calculation of repeatability. For the result with deviation -0,94 INR, the duplicate measurements gave reproducible values. Differences of this character are discussed in section 6.3.4.

Conclusion

Under real-life conditions the quality goal for accuracy was not fulfilled.

6.5. Evaluation of user-friendliness

6.5.1. Questionnaire to the evaluators

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

At the end of the evaluation period, the intended users filled in a questionnaire about the user-friendliness of the measurement system. SKUP has prepared detailed instructions for this.

The questionnaire is divided into four subareas:

Table A) Rating of the information in the manual / insert / quick guide
Table B) Rating of operation facilities. Is the system easy to handle?
Table C) Rating of time factors for the preparation and the measurement
Table D) Rating of performing internal and external analytical quality control

The intended users filled in table A and B. SKUP filled in table C and D and in addition, topics marked with grey colour in table A and B.

In the tables, the first column shows what is up for consideration. The second column in table A and B shows the rating by the users at the evaluation sites. The last three columns show the rating options. The overall ratings from all the evaluating sites are marked in coloured and bold text. The last row in each table summarises the total rating in the table. 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 on 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 will be discussed and taken into account in the overall assessment of the user-friendliness.

Comment
In this evaluation, the user-friendliness was assessed by PHCC1 (the opinion of three health secretaries and one medical secretary) and PHCC2 (the opinion of four health secretaries and one nurse).

Table A. Rating of the information in the manual and quick guide

Topic	Rating	Assessment	Assessment	Assessment
Table of contents/Index	**S, S**	**Satisfactory**	Intermediate	Unsatisfactory
Preparations / Pre-analytic procedure	**S, S**	**Satisfactory**	Intermediate	Unsatisfactory
Specimen collection	**S, S**	**Satisfactory**	Intermediate	Unsatisfactory
Measurement procedure	**S, S**	**Satisfactory**	Intermediate	Unsatisfactory
Reading of result	**S, S**	**Satisfactory**	Intermediate	Unsatisfactory
Description of the sources of error	**S, S**	**Satisfactory**	Intermediate	Unsatisfactory
Help for troubleshooting	**S, S**	**Satisfactory**	Intermediate	Unsatisfactory
Readability / Clarity of presentation	**S, S**	**Satisfactory**	Intermediate	Unsatisfactory
General impression	**S, S**	**Satisfactory**	Intermediate	Unsatisfactory
Measurement principle	**I**[1]	Satisfactory	Intermediate	**Unsatisfactory**
Available insert in Danish, Norwegian, Swedish	**S**	**Satisfactory**	Intermediate	Unsatisfactory
Total rating by SKUP		**Satisfactory**		

[1]There is no explanation of the measurement principle/reaction in the test strip

Additional positive comments:

- Nice and informative pictures in the quick guide, and a complement for the lamination of it.
- Good instructions during start-up led to less need for reading the manual or the insert.

Table B. Rating of operation facilities

Topic	Rating	Assessment	Assessment	Assessment
To prepare the test / instrument	**S, S**	**Satisfactory**	Intermediate	Unsatisfactory
To prepare the sample	**S, S**	**Satisfactory**	Intermediate	Unsatisfactory
Application of specimen	**S, S**	**Satisfactory**	Intermediate	Unsatisfactory
Specimen volume	**S, S**	**Satisfactory**	Intermediate	Unsatisfactory
Number of procedure step	**S, S**	**Satisfactory**	Intermediate	Unsatisfactory
Instrument / test design	**S, S**	**Satisfactory**	Intermediate	Unsatisfactory
Reading of the test result	**E, I**[1]	**Easy**	**Intermediate**	Difficult
Sources of errors	**I**[2]**, S**	**Satisfactory**	**Intermediate**	Unsatisfactory
Cleaning / Maintenance	**S, S**	**Satisfactory**	Intermediate	Unsatisfactory
Hygiene, when using the test	**S, S**	**Satisfactory**	Intermediate	Unsatisfactory
Size and weight of package	**S, S**	**Satisfactory**	Intermediate	Unsatisfactory
Storage conditions for tests, unopened package	**S**	**+15 to +30°C**	+2 to +8°C	–20°C
Storage conditions for tests, opened package	**S**	**+15 to +30°C**	+2 to +8°C	–20°C
Environmental aspects: waste handling	**S**	**No precautions**	Sorted waste	Special precautions
Intended users	**S**	**Health care personnel or patients**	Laboratory experience	Biomedical laboratory scientists
Total rating by SKUP		**Satisfactory**		

[1]The result disappeared rather quickly from the screen.
[2]Some error messages in cases when we were insecure if there was enough blood for the test strip. This was, however reassuring.

Additional positive comments:

- It is positive that there is no need for wire connected to the instrument. It is easy to fill the test strip with blood and a hygienic way to remove the test strip from the instrument.
- The system is easy to operate and it is user-friendly.

Table C. Rating of time factors (filled in by SKUP)

Topic	Assessment	Assessment	Assessment
Required training time	**<2 hours**	2 to 8 hours	>8 hours
Durations of preparations / Pre-analytical time	**<6 min.**	6 to 10 min.	>10 min.
Duration of analysis	**<10 min.**	10 to 20 min.	>20 min.
Stability of test, unopened package	**>5 months**	3 to 5 months	<3 months
Stability of test, opened package	**>30 days**	14 to 30 days	<14 days
Stability of quality control material, unopened	**>5 months**	3 to 5 months	<3 months
Stability of quality control material, opened	**>6 days or disposable**	2 to 6 days	≤1 day
Total rating by SKUP	**Satisfactory**		

Table D. Rating of analytical quality control (filled in by SKUP)

Topic	Assessment	Assessment	Assessment
Reading of the internal quality control	**Satisfactory**	Intermediate	Unsatisfactory
Usefulness of the internal quality control	**Satisfactory**	Intermediate	Unsatisfactory
External quality control	**Satisfactory**	Intermediate	Unsatisfactory
Total rating by SKUP	**Satisfactory**		

6.5.2. Assessment of the user-friendliness

Assessment of the information in the manual (table A)
The manual and quick guide was assessed as satisfactory with a positive comment regarding informative illustrations in the quick guide.

Assessment of the operation facilities (table B)
The operation facilities were in total assessed as satisfactory, although Xprecia Stride reported relatively many error messages related to the handling of the sample (5,6%), see 6.1. However, the evaluators did not consider this as difficulties caused by the system, but rather as a result of the sampling situation.

Assessment of time factors (table C)
The time factors were assessed as satisfactory.

Assessment of analytical quality control possibilities (table D)
The analytical quality control possibilities were assessed as satisfactory.
The imprecision achieved with the internal analytical control material (PT Control 1 and PT Control 2), equals the imprecision of the patient samples.

Conclusion
In all, the user-friendliness of Xprecia Stride and its manual was rated as satisfactory. The quality goal for user-friendliness was fulfilled.

7. References

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Attachments

1. The organisation of SKUP
2. Facts about Xprecia Stride
3. Information about manufacturer, retailers and marketing
4. Product specifications for this evaluation, Xprecia Stride
5. Statistical expressions and calculations
6. Raw data PT (INR), results from the comparison method
7. Raw data PT (INR), internal analytical quality control results, Xprecia Stride, optimal conditions
8. Raw data PT (INR), Xprecia Stride results, optimal conditions
9. Raw data PT (INR), internal analytical quality control results, Xprecia Stride, intended users
10. Raw data PT (INR), Xprecia Stride results, intended users
11. "SKUP-info". Summary for primary health care (in Norwegian)
12. List of previous SKUP evaluations
13. Comments from Siemens Healthcare Diagnostics INC

Attachments with raw data are included only in the copy to Siemens Healthcare Diagnostics AS.

The organisation of SKUP

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

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

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

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

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

SKUP reports are published at www.skup.nu.

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

[2] SKUP in Denmark is placed in Nordsjællands Hospital. Currently SKUP in Denmark is out of operation due to lack of funding.

[3] Equalis AB (External quality assessment for clinical laboratory investigations in Sweden) is a limited company in Uppsala, Sweden, owned by “Sveriges Kommuner och Landsting” (Swedish Association of Local Authorities and Regions), “Svenska Läkaresällskapet” (Swedish Society of Medicine) and IBL (Swedish Institute of Biomedical Laboratory Science).

Facts about Xprecia Stride

Parts of this form are filled in by Siemens Healthcare Diagnostics AS

Table 1. Basic facts

Name of the measurement system:	Xprecia Stride™ Coagulation Analyzer
Dimensions and weight:	Width: 70 mm Depth: 40 mm Height: 170 mm Weight: 300 g
Components of the measurement system:	Analyzer, single use test strips and optional liquid controls
Measurand:	PT (INR)
Sample material:	Fresh capillary whole blood
Sample volume:	6 µl
Measuring principle:	Electrochemical
Traceability:	To the WHO tilt tube standard
Calibration:	Happens automatically with bar-code scanning of test strip vials
Measuring range:	0.8 – 8 INR
Linearity:	
Measuring time:	Varies from a few seconds to 96 seconds depending on status of anticoagulation of sample
Operating conditions:	Temperature from 15ºC to 35ºC. Relative humidity 20-80%.
Electrical power supply:	Disposable alkaline batteries. Rechargeable nickel metal batteries.
Recommended regular maintenance:	External cleaning and disinfection between patients recommended
Package contents:	Analyzer kit includes analyzer, color caps, batteries, USB cable and product instructional materials
Necessary equipment not included in the package:	Test strips are sold separately. Liquid control solutions are sold separately.

Table 2. Post analytical traceability

Is input of patient identification possible?	Yes, a patient ID can be entered via the onboard bar-code scanner or manually typed via the analyzer touchscreen
Is input of operator identification possible?	Yes, similar to above, Operator ID can be scanned or entered manually via the touch screen.
Can the instrument be connected to a bar-code reader?	Bar-code is integrated as part of the analyzer
Can the instrument be connected to a printer?	No, not directly but results can be downloaded to a PC via the integrated USB port and once downloaded it can be printed
What can be printed?	Once data is downloaded to a PC, all data can be printed
Can the instrument be connected to a PC?	Yes

Can the instrument communicate with LIS (Laboratory Information System)? If yes, is the communication bidirectional?	Communication to LIS is possible and communication is bi-directional
What is the storage capacity of the instrument and what is stored in the instrument?	A minimum of 640 patient test results, 300 liquid quality controls, 300 error messages
Is it possible to trace/search for measurement results?	Yes, past results may be reviewed from analyzer memory

Table 3. Facts about the reagent/test strips/test cassettes

Name of the reagent/test strips/test cassettes:	Xprecia™ PT/INR Strips
Stability in unopened sealed vial:	24 months
Stability in opened vial:	3 months
Package contents:	4 vials of 25 test strips each

Table 4. Quality control

Electronic self-check:	Yes.
Recommended control materials and volume:	Xprecia PT liquid controls, volume of 6 µL per test
Stability in unopened sealed vial:	Minimum of 12 months
Stability in opened vial:	25 minutes
Package contents:	4 Vials of Level 1, 4 Vials of Level 2 and 8 vials of diluent

Information about manufacturer, retailers and marketing

Table 1. Marketing information

Manufacturer:	Siemens Healthcare Diagnostics Inc., 511 Benedict Avenue, Tarrytown, NY 10591-5097 USA
Retailers in Scandinavia:	Denmark: Abena A/S and Mediq Denmark A/S Norway: Siemens Healthcare Diagnostics AS Sweden: Mediq Sweden AB
In which countries is the system marketed:	Globally and currently under FDA review and Health Canada review
Date for start of marketing the system in Scandinavia:	Autumn 2015
Date for CE-marking:	December 8, 2014
In which Scandinavian languages is the manual available:	Norwegian, Swedish, Danish

Product specifications for this evaluation, Xprecia Stride

Xprecia Stride serial numbers

Instrument/Ref.	Serial number	Used by
Xprecia Stride/10714596	101345	SKUP
Xprecia Stride/10714596	101503	PHCC1
Xprecia Stride/10714596	101431	PHCC2
Xprecia Stride/10714596	101370	extra

Xprecia Stride test strips

Lot number	Expiry date	Used by
400574	2017-01-19	SKUP, PHCC1, PHCC2
400587	2017-02-06	SKUP, PHCC1, PHCC2
400589	2017-02-09	SKUP, PHCC1, PHCC2

Other equipment used in the evaluation

Other equipment	Lot number	Expiry date	Used by
BD Vacutainer 9NC 0,109 M Na3Citrate, Ref. 363048	5180189	2016-03	SKUP, PHCC1, PHCC2
PT Controls, Ref. 10873436	45016 and 45620	2016-02-08 and 2017-06-21	SKUP, PHCC1, PHCC2
Cutisoft Wipes skin clean, Ref. 72383-01	525154	2019-05	SKUP, PHCC1, PHCC2
Accu-Chek Safe-T-Pro Plus lancet, Ref. 03603539150	41515166	2019-08	SKUP, PHCC1, PHCC2
Vacutainer eclipse Blood collection needle21Gx1-1/4” (0,8x3,2 mm), Ref. 368650	4188760	2017-07	SKUP

Statistical expressions and calculations

This chapter 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 ISO/IEC Guide 99; International Vocabulary of Metrology, 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. A measurement is said to be more accurate when it offers a smaller measurement error. Accuracy can be illustrated in a difference-plot. Accuracy is descriptive in general terms (good, poor e.g.).

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

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]:

$$SD = \sqrt{\frac{\sum d^2}{2n}}$$

d = difference between two paired measurements
n = number of differences

(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:

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

m = mean of paired measurements

(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 based on results achieved under optimal measuring conditions. A paired t-test is used with the mean values of the duplicate results on the comparison method and the mean values 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 quality goal limits is counted and assessed.

b. Burnett RW. Accurate estimation of standard deviations for quantitative methods used in clinical chemistry. Clinical Chemistry 1975; **21** (13): 1935 – 1938.
c. Saunders E. Tietz textbook of clinical chemistry and molecular diagnostics, 2006. Chapter 14, Linnet K., Boyd J. Selection and analytical evaluation of methods – with statistical techniques. Elsevier Saunders ISBN 0-7216-0189-8.
d. Fraser C.G. Biological variation: From principles to practice, 2006. Chapter 1, The Nature of Biological Variation. AACC Press ISBN 1-890883-49-2.

SKUP-info

Sammendrag av en utprøving i regi av SKUP
Xprecia Stride™ for måling av PT-INR
Produsent: Siemens Healthcare Diagnostics INC
Norsk forhandler: Siemens Healthcare Diagnostics AS

Konklusjon
Totalt sett var variasjonskoeffisienten (CV) i overkant av 5% og kvalitetsmålet for presisjon ble ikke oppfylt. Kvalitetsmålet for nøyaktighet ble ikke oppfylt. Kvalitetsmålet for brukervennlighet ble oppfylt.

Bakgrunn
Xprecia Stride er et bærbart koagulometer for måling av protrombintid, PT-INR. Systemet er beregnet for helsepersonell til oppfølging av pasienter som behandles med warfarin. Prøvematerialet er ferskt kapillært fullblod. Instrumentet produseres av Siemens Healthcare Diagnostics INC og ble lansert i det skandinaviske markedet høsten 2015. Denne SKUP-utprøvingen ble utført i perioden desember 2015 til mars 2016 på oppdrag fra Siemens Healthcare Diagnostics AS i Norge.

Utprøvingen
Målet med utprøvningen var å bestemme den analytiske kvaliteten og brukervennligheten til Xprecia Stride, både i bruk under optimale forhold av erfarent laboratoriepersonell og under reelle forhold av brukerne i primærhelsetjenesten. Resultatene ble vurdert i forhold til kvalitetsmål satt av SKUP i forkant av utprøvingen.

Material og metode
Under optimale forhold ble det analysert kapillære prøver fra 101 pasienter på Xprecia Stride (en modifisert Quick-metode). To legekontor analysert kapillære prøver fra 40 pasienter hver. Resultatene fra Xprecia Stride ble sammenlignet med resultatene fra en anerkjent sykehusmetode (Owren-metode, STA-R Evolution, STAGO) for måling av PT-INR i plasma. For presisjon var kvalitetsmålet en CV≤ 5,0 % og for nøyaktighet at ≥95 % av resultatene fra Xprecia Stride skulle avvike mindre enn 20 % fra resultatene fra sammenligningsmetoden. Kvalitetsmålet for brukervennlighet var at den totale vurderingen skulle være tilfredsstillende.

Resultat
For resultat under 2,5 INR var CV under optimale forhold 4,7 %, og henholdsvis 4,5 % and 5,5 % ved de to legekontorene. For resultat over 2,5 INR var CV 5,3 % under optimale forhold og 6,4% and 7,1% ved de to legekontorene. For resultat under 2,5 INR, ble det både under optimale forhold og ved legekontorene påvist en negativ bias mellom Xprecia Stride og sammenligningsmetoden i størrelsesorden fra (-0,09) – (-0,17) INR. For resultat over 2,5 INR ble det påvist en bias på -0,23 INR ved ett av legekontorene. Under optimale forhold var 93 % av resultatene innenfor grensen for tillatt avvik. Hos brukerne på de to legekontorene var 92 % av resultatene innenfor grensen. Brukervennligheten ble vurdert som tilfredsstillende. Totalt ble 0,3 % av teststrimlene forkastet pga. tekniske feil.

Tilleggsinformasjon
Fullstendig rapport fra utprøvingen av Xprecia Stride, SKUP/2016/110, finnes på SKUPs nettside www.skup.nu. Laboratoriekonsulentene i Noklus kan gi råd om analysering av PT-INR på legekontor. De kan også orientere om det som finnes av alternative metoder/utstyr.

List of previous SKUP evaluations

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

The 30 latest SKUP evaluations

Evaluation no.	Component	Instrument/test kit	Producer
SKUP/2016/110	PT (INR)	Xprecia Stride Coagulation system	Siemens Healthcare Diagnostics INC
SKUP/2015/107	Strep A	QuickVue Dipstick Strep A Test	Quidel Corporation
SKUP/2015/109	PT (INR)	microINR portable coagulometer	iLine Microsystems S.L.
SKUP/2015/108	HbA1c	*Confidential*	
SKUP/2015/102	HbA1c	*Confidential*	
SKUP/2015/106*	Strep A	QuikRead go	Orion Diagnostica Oy
SKUP/2014/101	HbA1c	InnovaStar analyzer	DiaSys Diagnostic Systems GmbH
SKUP/2014/104	PT (INR)	ProTime InRythm	ITC International Technidyne Corporation
SKUP/2014/105	Glucose[1]	Accu-Chek Aviva	Roche Diagnostics
SKUP/2014/103	PT (INR)	*Confidential*	
SKUP/2013/87	Glucose[1]	Wella Calla Light	Med Trust Handelsges.m.b.H.
SKUP/2013/100	Glucose[1]	Mylife Unio	Bionime Corporation
SKUP/2013/97	NT-proBNP	Cobas h 232 POC system	Roche Diagnostics GmbH
SKUP/2013/92	CRP	Eurolyser smart 700/340	Eurolyser Diagnostica GmbH
SKUP/2013/99*	Glucose	Accu-Chek Mobile	Roche Diagnostics
SKUP/2013/98*	Glucose	Accu-Chek Aviva	Roche Diagnostics
SKUP/2013/85	Glucose, β-Ketone	Nova StatStrip	Nova Biomedical Corporation, USA
SKUP/2013/96	Hemoglobin	DiaSpect Hemoglobin T	DiaSpect Medical GmbH
SKUP/2013/68	Allergens	ImmunoCap Rapid	Phadia AB Marknadsbolag Sverige
SKUP/2012/95	Glucose[1]	Mendor Discreet	Mendor Oy
SKUP/2012/94	Glucose[1]	Contour XT	Bayer Healthcare
SKUP/2012/91	HbA1c	Quo-Test A1c	Quoient Diagnostics Ltd
SKUP/2011/93*	Glucose	Accu-Chek Performa	Roche Diagnostics
SKUP/2011/90	CRP	*i*-Chroma	BodiTech Med. Inc.
SKUP/2011/84*	PT (INR)	Simple Simon PT and MixxoCap	Zafena AB
SKUP/2011/86	Glucose[1]	OneTouch Verio	LifeScan, Johnson & Johnson
SKUP/2011/77	CRP	*Confidential*	
SKUP/2011/70*	CRP	smartCRP system	Eurolyser Diagnostica GmbH
SKUP/2010/83*	Glucose	*Confidential*	
SKUP/2010/78	HbA1c	In2it	Bio-Rad

*A report code followed by an asterisk indicates that the evaluation is not complete according to SKUP guidelines, since the part performed by the intended users was not included in the protocol, or the evaluation is a follow-up of a previous evaluation, or the evaluation is a special request from the supplier.
[1] Including a user-evaluation among diabetes patients

SIEMENS Healthcare

SKUP
Noklus Centre
Att: **Anne Christin Breivik**
Boks 6165
5892 Bergen, NORWAY

June 2, 2016

RE: Comments on the SKUP Evaluation Report on the Xprecia Stride™ Coagulation Analyzer

Dear Ladies and Gentlemen,

Thank you for providing the evaluation report on the Xprecia Stride Coagulation Analyzer and for the opportunity to provide additional commentary to the written report.

We appreciate the mention of potential factors that may have contributed to the comparison between a whole blood point-of-care system and a plasma-dilution laboratory method.

Repeatability
The SKUP standard for overall repeatability is ≤5% CV. The Xprecia Stride analyzer results were slightly above 5% but we are pleased to see that the difference is not statistically significant since the confidence intervals include 5% as stated in the report on pages 20 and 22.

Accuracy
We are also pleased to see the Xprecia Stride analyzer performance is not statistically significantly different than the SKUP quality goal of 95% of samples within ± 20% of the reference device.

Usability
We were happy to read, that in a primary-care setting, the evaluation confirmed excellent ease of use, specifically highlighting good instructions on start-up, which reduce the need to keep referring to the manual. We are particularly pleased that the users made positive comments regarding the safety features of easy to fill strip and the unique eject button to remove the test strip from the instrument.

We feel that the comments demonstrate we are meeting customer expectations for good quality, highly usable analyzers with important safety features. Additionally the low strip rate failure of 0.3% has two outcomes; it helps to minimize costs associated with retesting for the customer and prevents the inconvenience of retesting to the patient.

Siemens Healthcare is committed to producing high-quality products that are easy to use to enable real time decisions in patient care. All comments and feedback are appreciated as we continually strive to improve our Xprecia product line.

Best Regards,
Siemens Healthcare

Sue Degnan
VP, Assay Development

Arnol S. Rios
Sr. Manager, Global Marketing, Sales & Communications

Siemens Healthcare Diagnostics Inc.

2 Edgewater Drive
Norwood, MA 02062
USA

Tel.: +1 781 269-3000
Fax: +1 781 269-3599