LabPad Evolution

A system for measurement of CRP, (PT) INR, d-dimer and fibrinogen manufactured by Biosynex SA

An evaluation of the measurement of CRP

Report from the evaluation

SKUP/2024/136

organised by SKUP at the request of Biosynex Nordic A/S

www.skup.org

SKUP Scandinavian evaluation of laboratory equipment for point of care testing

SKUP secretariat
Christine Morken
+47 404 72 928
christine.morken@noklus.no

SKUP in Denmark
Dår Kristian Kur
Gitte M. Henriksen
DEKS
+45 38 63 44 06
daar.kur@deks.dk

SKUP in Sweden
Elisabet Eriksson Boija
Anna Karlsson
Equalis AB
+46 18 490 31 44
elisabet.eriksson.boija@equalis.se

SKUP in Norway
Christine Morken
Joakim Hekland
Silje Bryn Ekehaug
Anne Stavelin
Sverre Sandberg
Noklus
+47 404 72 928
christine.morken@noklus.no
joakim.hekland@noklus.no
silje.ekehaug@noklus.no

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Attachments with raw data are included only in the copy to Biosynex Nordic A/S.

1. Summary

LabPad Evolution Ksmart CRP

Manufacturer	Biosynex SA
Supplier in Scandinavia	Biosynex Nordic A/S
Launched in Scandinavia	November 2022

Aim

To assess the analytical performance and user-friendliness of CRP measurements with LabPad Evolution when used by the intended users, i.e. health care professionals, in primary health care.

Performance specifications		**Conclusion and results**
Repeatability	CV ≤10 %	Not fulfilled when used by the intended users. (CV 18,6 – 24,8 %)
Accuracy ≥95 % of the results within the specified limits compared to the average result of the comparison method	±2 mg/L at CRP concentration <10 mg/L ±15 % at CRP concentration ≥10 mg/L	Not fulfilled when used by the intended users. (80,6 %)
User-friendliness	A total rating of "Satisfactory"	Not fulfilled. The user-friendliness was rated *intermediate*.

Additional information

Participants	186 participants from five primary health care centres, coming in with symptoms of infection where the general practitioner requested a CRP measurement.
Evaluated method	LabPad Evolution Ksmart CRP (immunofluorescence) on fresh capillary whole blood using three lots of test kits. Intended for professional use.
Comparison method	Cobas 8000, c 702 (particle-enhanced immunoturbidimetric assay) on venous serum samples.
Bias	An average small positive bias of 0,29 mg/L between LabPad Evolution and the comparison method was shown.
Technical error	0,38 %. The SKUP recommendation of a fraction of ≤2 % was achieved.

A letter with comments from Biosynex Nordic A/S 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 SKUPs website.

2. Abbreviations and Acronyms

APS	Analytical performance specification
BLS	Biomedical Laboratory Scientist
C-NPU	Committee on Nomenclature, Properties and Units
CI	Confidence Interval
CRP	C-reactive protein
CV	Coefficient of Variation
DEKS	Danish Institute of External Quality Assurance for Laboratories in the Health Sector
EFLM	European Federation of Clinical Chemistry and Laboratory Medicine
ERM	European Reference Materials
EQA	External Quality Assessment
Equalis	External quality assessment in laboratory medicine in Sweden
IFCC	International Federation of Clinical Chemistry and Laboratory Medicine
Noklus	Norwegian Organization for Quality Improvement of Laboratory Examinations
PHCC	Primary health care centre
POC	Point of care
QC	Quality control
SKUP	Scandinavian evaluation of laboratory equipment for point of care testing

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 comparable[1]. 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 end-users should be involved in the evaluation. If possible, SKUP evaluations are carried out using three lot numbers of test kits 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 evaluation

The LabPad Evolution system is an in vitro diagnostic device for the measurement of C-reactive protein (CRP), (PT) INR, d-dimer and fibrinogen. The product is intended for use by health care professionals. The sample material for measurement of CRP is capillary whole blood and venous heparin anticoagulated whole blood and plasma. The measuring system is produced by Biosynex SA and was launched into the Scandinavian market November 2022. The SKUP evaluation was carried out from August to November 2023 at the request of Biosynex A/S in Denmark.

3.3. The aim of the evaluation

The aim of the evaluation was to assess the analytical performance and user-friendliness of LabPad Evolution Ksmart CRP, when used by intended users in primary health care.

3.4. The model for the evaluation of LabPad Evolution Ksmart CRP

SKUP evaluations for quantitative methods are based upon the fundamental guidelines in a book concerning evaluations of laboratory equipment in primary health care [1].
SKUP's model for CRP evaluations (figure 1) focus on POC device performance among the intended users in primary health care. Five primary health care centres (PHCCs) participated in the evaluation and the evaluation document the performance of the measuring system when used by the intended users.

The evaluation included:

- Examination of the analytical performance (precision and accuracy) in the hands of intended users.
- Evaluation of the user-friendliness of LabPad Evolution Ksmart CRP and its manual.
- Examination of the reproducibility of the LabPad Evolution Ksmart CRP in heparin plasma.

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

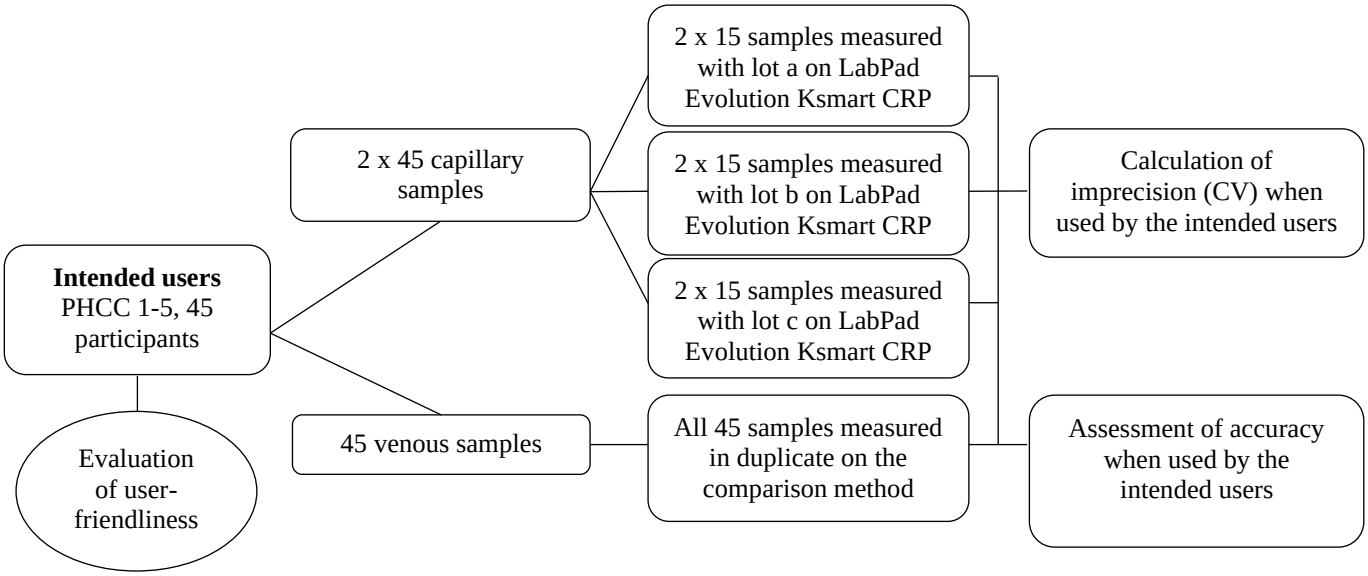

Figure 1. Flowchart illustrating the model for the evaluation of LabPad Evolution Ksmart CRP in capillary samples. The same procedure was performed in five different PHCCs.

4. Performance specifications

4.1. Analytical performance specifications

The 1st European Federation of Clinical Chemistry and Laboratory Medicine (EFLM) Strategic Conference, held in 2014 in Milan, defined three models to be used to derive analytical performance specifications (APSs) [2]. Ceriotti *et al.* [3] give criteria for allocating measurands to the different models for APSs recognized in the EFLM Strategic Conference and propose a theoretical rationale for selecting the best model that should be applied to a specific measurand.

International guidelines for quality requirements for CRP are few. According to the discussion about advantages and disadvantages of the three models for various measurands the EFLM Strategic Conference defined, the APSs for CRP in this SKUP evaluation will be based on Model 3; state of the art [3]. There is no official agreement on how to set APSs based on this model, but a possible way is to derive them from external quality assessment (EQA) programs.

The National Danish Committee for general practice Laboratory testing appointed by the National Ministry of health has specified the demands to quality goals; bias and imprecision (coefficient of variation, CV), for CRP instruments used in primary health care [4]. The Danish goals also include demands to the comparison method.
Analytical quality goals for CRP >15 mg/L:

Near patient tests used in primary health care centres	bias ≤±10 % and CV ≤10 %
Hospital laboratory methods used as a comparison method	bias ≤±3 % and CV ≤5 %

In the external quality assessment programme offered by the Norwegian organization for quality improvement of laboratory examinations (Noklus), the following limits for deviation are in use for CRP in primary health care: To achieve the assessment *good*, the maximum deviation from the control target value should be less than approximately ±8 %, depending on the CRP concentration in the control sample. A deviation between 8 and 15 % gives the assessment *acceptable*.

For near patient tests used in primary health care centres the advisory group of protein analysis in the External quality assessment in laboratory medicine in Sweden (Equalis) suggest that the maximum deviation for a single result measured in whole blood should be ±15 % when compared to an assigned value set by five agreeing hospital laboratory methods for separated plasma. For hospital methods the maximum deviation for a single result measured in plasma should be ±10 % when compared to an assigned value set as the mean of five agreeing group means.

Based on recommendations from professionals and results in the Equalis and Noklus EQA programs, SKUP's APSs for CRP in this evaluation are as presented in section 4.4.

4.2. User-friendliness

The evaluation of user-friendliness was carried out by asking the evaluating persons to fill in a questionnaire, see section 6.4.

Technical errors
SKUP recommends that the fraction of tests wasted due to 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 performance as well as satisfactory user-friendliness.

4.3.1. 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, was 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 does 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 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 test kits were visually shown in the assessment of accuracy in the difference plot for the results achieved when used by the intended users of the measuring system. If distinct differences between the lots appeared, this was pointed out and discussed.

Accuracy

The accuracy was illustrated in a difference plot 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.

4.3.2. Assessment of the user-friendliness

The user-friendliness was assessed according to the answers and comments given in the questionnaire (see section 6.4). For each question, the evaluator could choose between three given ratings; satisfactory, intermediate and unsatisfactory. The responses from the evaluators were reviewed and summed up. To achieve the overall rating "satisfactory", the tested equipment must reach a total rating of "satisfactory" in all four subareas of characteristics described in section 6.4.

Technical errors

The evaluating persons registered error codes, technical errors and failed measurements during the evaluation. The fraction of tests wasted due to technical errors were calculated and taken into account in connection with the assessment of the user-friendliness. User errors were not included in the calculation.

4.4. SKUP's performance specifications in this evaluation

As agreed upon when the protocol was drawn up, the results from the evaluation of LabPad Evolution Ksmart CRP were assessed against the following performance specifications:

Repeatability (CV)…..... ≤10 %

Allowable deviation of the individual result from the comparison method result
for CRP concentrations < 10 mg/L..... ≤±2,0 mg/L
and for CRP concentrations ≥10 mg/L..... ≤±15 %

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

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

5. Materials and methods

5.1. Definition of the measurand

The measuring systems intend to measure the mass concentration of CRP in plasma. For the evaluated measuring system, the sample material in this evaluation was fresh whole blood capillary samples, and for the comparison method the sample material was serum. The results are traceable to the European Reference Material (ERM)-DA472/International Federation of Clinical Chemistry and Laboratory Medicine (IFCC) [5] and are expressed in the unit mg/L. The Committee on Nomenclature, Properties and Units (C – NPU) systematically describes clinical laboratory measurands in a database [6]. The NPU code related to the measurand in this evaluation is NPU19748. In this report the term CRP will be used for the measurand.

5.2. The evaluated measuring system LabPad Evolution Ksmart CRP

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

The LabPad Evolution is a system intended for POC testing for health care professionals. The LabPad Evolution is compatible with Tsmart and Ksmart test cassettes, called SmartChips. Analytes available for testing on LabPad Evolution is (PT) INR, CRP, d-dimer and fibrinogen. The LabPad Evolution system with Ksmart CRP includes:

Figure 2. LabPad Evolution with Ksmart SmartChip

- LabPad Evolution reader
- Charger and micro-USB-B-cable
- Carry bag for the LabPad Evolution
- Instructions for use
- Ksmart CRP test cassettes*
- Buffer tubes*
- End-to-end capillary pipettes*
- Quality control, 2 levels, consisting of*
    - 2 pre-filled bottles for "low" level CRP control reconstitution
    - 2 pre-filled bottles for "high" level CRP control reconstitution
    - 4 lyophilized CRP control beads

*Part of test kit to be bought separately.

LabPad Evolution with Ksmart CRP is an in vitro diagnostic test system designed to quantitatively determine CRP in human capillary whole blood as well as heparin anticoagulated venous whole blood and plasma.

The measurement principle for LabPad Evolution Ksmart CRP is immunofluorescence. The test kit consists of a sampling buffer, a reaction buffer and a reaction membrane on the test cassette. The reaction buffer contains monoclonal anti-CRP antibodies with fluorescence label. The reaction membrane contains secondary monoclonal anti-CRP antibodies.

When the sample material is added to the test well on the test cassette, the conjugate in the reaction buffer will mix with the sample. If there is CRP present in the sample, a reaction product with the monoclonal antibodies marked with fluorescence will be formed. The reaction product

will migrate on the nitrocellulose membrane on the reaction membrane to the detection line. On the detection line secondary monoclonal antibodies will catch the reaction product, which creates the end reaction. The excitation light will mark a red line where the end products are, which will be detected by the instrument. The reaction membrane also contains a control line, that ensures that correct amount of sample is added to the test, and that the membrane is working correctly.

For technical details about the LabPad Evolution Ksmart CRP, see table 2. For more information about the LabPad Evolution Ksmart CRP measuring system, and name of the manufacturer and the suppliers in the Scandinavian countries, see attachment 1 and 2. For product specifications in this evaluation, see attachment 3.

Table 2. Technical details from the manufacturer.

Technical details for LabPad Evolution Ksmart CRP	
Sample material	Capillary whole blood, venous heparin whole blood or plasma
Sample volume	10 µL
Measuring time	2 minutes
Measuring range	0,5 mg/L – 200 mg/L
LIS communication	Yes
Storage capacity	1000 results

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 was the routine method for CRP measurement at the Department of medical biochemistry and pharmacology, section for automated analyses at Haukeland University hospital, hereafter called "the comparison method".

Instrument:	cobas 8000, c 702
Reagent:	CRP4, Tina-quant C-Reactive Protein IV
Principle:	Particle-enhanced immunoturbidimetric assay, determination at absorbance level 570 nm
Traceability:	Traceable to ERM-DA474/IFCC
Calibrators:	S1: H_2O S2-S6: Calibrator f.a.s. Proteins from Roche
Measuring range:	Lowest value: <3 mg/L Highest value: results >350 mg/L is automatically diluted 1:2 by the instrument.

Internal analytical quality control

Internal analytical quality control samples, three levels (Autonorm Human Liquid L-2 and L-3, Sero AS, and Liquicheck CRP 3, Bio-Rad Laboratories Inc.), were measured daily on the comparison method.

External analytical quality control

The hospital laboratory participates in Noklus EQA scheme for CRP with two levels in four rounds per year. The materials are freshly frozen pooled plasma from healthy Norwegian donors with added purified human CRP. The assigned value for CRP is based on transferred reference values from ERM-DA474/IFCC [5].

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 the venous serum samples from each participant.

Trueness

The trueness of the comparison methods was verified with EQA results.

5.4. The evaluation

5.4.1. Planning of the evaluation

Inquiry about an evaluation

Biosynex A/S via Preben Joffe, Global Chief Medical Director, applied to SKUP in February 2023 for an evaluation of LabPad Evolution Ksmart CRP.

Protocol, arrangements and contract

In May 2023, the protocol for the evaluation was approved, and Biosynex A/S and SKUP signed a contract for the evaluation. Five PHCCs, Legehuset Varden, Minde Medisinske Senter, Volvat Medisinske Senter, Nesttun Legekontor and Strandsiden Legesenter from Bergen, Norway, agreed to represent the intended users in this evaluation. Nesttun Legekontor had to withdraw from the evaluation in October 2023, and was replaced by Strandsiden Legesenter.

Training

Biosynex A/S was responsible for the training of the PHCCs, except for the training of Strandsiden Legesenter which was trained by SKUP in close collaboration with Biosynex A/S. The training in the PHCCs reflected the training usually given to the end-users. Biosynex A/S 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 18 weeks in the PHCCs, ending in December 2023. At the Department of Clinical Biochemistry and Pharmacology, Haukeland University Hospital, biomedical laboratory scientists (BLSs) were responsible for the comparison method as described in section 5.3.1. The laboratory has approximately 27 employees. Depending on the PHCC, two or three health care secretaries participated in the evaluation. The PHCCs have between 5 and 8 physicians. All PHCCs collects capillary samples in routine, but only three of them use capillary samples in routine for CRP measurements.

5.4.3. The evaluation procedure for intended users

Internal analytical quality control

Internal analytical quality control samples for LabPad Evolution Ksmart CRP, 2 levels (Ksmart CRP + Controls, Biosynex SA) were measured each evaluation day on LabPad Evolution. The reproducibility (CV) as achieved with the quality control material was calculated.

Recruitment of participants and ethical considerations

People, 18 years or older, coming to the PHCC with symptoms of infection, where the general practitioner requested a CRP measurement, were asked if they were willing to donate two capillary and one venous blood sample for the evaluation. Participation was voluntary and verbal informed consent was obtained from the participants. No personal information about the participants was obtained in the evaluation. An ethical approval was not necessary because the evaluation was considered as a quality assurance project.

It was desirable that approximately 30 % of the samples had a CRP result <20 mg/L, approx. 40 % of the samples had a CRP result between 20 and 60 mg/L and approx. 30 % of the samples had a CRP result >60 mg/L.

Handling of the samples and measurements
Fresh whole blood capillary samples were used for measurement with the LabPad Evolution measuring system. All measurements were performed in duplicate. The participants washed and dried their hands, and the puncture site was disinfected with alcohol pads and dried completely before sampling. Disposable lancing devices with depth settings 2,3 mm were used.
The first drop of blood was wiped off with a swab, and the second drop of blood was collected in the capillary included in the test kit. The capillary sample was added to the dilution bottle and mixed well for at least 30 seconds. The first drop from the dilution bottle was discarded, and the next two drops was dripped onto the test cassette. The test cassette remained at rest for the sample to migrate to the end of the cassette (1 minute), before the test cassette was inserted into the LabPad Evolution reader. The complete sampling and measurement procedure was repeated for the second measurement on LabPad Evolution, if possible from the same finger prick. In case of error codes, the test was repeated, if possible, until a result was obtained. Three lot numbers of test kits were used at each site during the course of the evaluation. The same lot number was used for measurement of internal analytical quality control and participant samples any given day.

Samples for the comparison method were obtained from venous puncture and collected into 5,0 mL Vacutainer serum separator tube with clot activation (BD). The tubes were inverted 8 times to ensure thorough mixing and kept in an upright position for 30 minutes in room temperature to clot. The tubes were centrifuged for 10 minutes at 1800 – 2200 g within two hours from sampling and kept at 4 – 8°C until transported to the hospital laboratory later the same day or the day after. The serum samples were measured in duplicate for CRP on the comparison method within 72 hours after collection. All samples were treated according to the internal procedures of the hospital laboratory regarding potential interfering substances.

5.4.4. The procedure for the evaluation of reproducibility

The reproducibility of LabPad Evolution Ksmart CRP in heparin plasma was performed by the Department of Clinical Biochemistry and Pharmacology, Haukeland University Hospital. Two heparin plasma pools with approximate concentrations of 10 mg/L and 100 mg/L were aliquoted in 10 aliquots and frozen at -80°C. One aliquot of each level was thawed, mixed and analysed on LabPad Evolution Ksmart CRP two times every day, for 10 days.

6. Results and discussion

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

6.1. Number of samples and study population characteristics

Scheduled number of samples in this evaluation was 180 participant samples measured in duplicate by intended users in PHCCs.
At the end of the evaluation, a total of 186 participants were enrolled. PHCC1 recruited 35 participants (SKUP ID 101 – 135), PHCC2 recruited 45 participants (SKUP ID 201 – 246), PHCC3 recruited 50 participants (SKUP ID 301 – 352), PHCC4 recruited 21 participants (SKUP ID 401 – 421), PHCC5 recruited 35 participants (SKUP ID 501 – 536). The results from the comparison method covered a CRP interval from 0,14 – 264,35 mg/L.
An account of the number of samples not included in the calculations, is given below.

Missing results

- In total for all PHCCs, internal quality control results for 15 evaluation days were missing.
  The results from the participant samples these days were still included in the calculations.
- ID 314; only single result from LabPad Evolution due to lack of migration on the test cassette on the second measurement. The single value was included in the calculation of bias and the assessment of accuracy.
- ID 237 and 350; only single measurement result from LabPad Evolution as one of the duplicates were reported to be <0,5 mg/L. The single value was included in the calculation of bias and the assessment of accuracy.
- ID 119; only single measurement result from LabPad Evolution as one of the duplicates were reported to be >200 mg/L. The single value was included in the calculation of bias and the assessment of accuracy.
- The results from ID 314, ID 237, ID 350 and ID 119 were included in the calculation of repeatability of the comparison method.

Omitted results

- SKUP ID 209 was omitted due to internal quality control outside of the allowable limits stated by the manufacturer. The result from this ID was only included in the calculation of repeatability of the comparison method.
- LabPad Evolution Ksmart CRP reports CRP results below 0,5 mg/L as <0,5 mg/L. Due to this, 6 results were not included in any calculations; ID 112, ID 304, ID 502, ID 503, ID 529, ID 534.
- LabPad Evolution Ksmart CRP reports CRP results over 200 mg/L as >200 mg/L. Due to this, four results were not included in any calculations; ID 228, ID 231, ID 338, ID 506.

Excluded results (statistical outliers)

Statistical outliers in SKUP evaluations are detected by the criterion promoted by Burnett [7]:

- ID 125, ID 236, ID 306, ID 317, ID 337, ID 405, ID 406 and ID 533; the results from LabPad Evolution 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 but the results were included in the assessment of accuracy (the first of the duplicate measurements).
- ID 104, ID 115, ID 119, ID 205, ID 224, ID 242 and ID 501; the results 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 assessment of accuracy (the first of the duplicate measurements) and repeatability (duplicate measurements).

Recorded error codes, technical errors and failed measurements
There was one report of failed measurement due to lack of migration on the test cassette, and one error code (error code 109) at PHCC3 on measurement of internal quality control. This amounts to 0,38 % (2 out of 186 x 2 participant samples and 151 internal quality control measurements) The SKUP recommendation of a fraction of ≤2 % tests wasted due to technical errors was achieved.

6.2. Analytical performance of the selected comparison method

6.2.1. Internal analytical quality control

All results from the internal analytical quality control (Autonorm Clin Chem Liq L-2 and L-3, and Liquicheck CRP 3), 3 levels, were within the allowable control limits (data not shown).

6.2.2. The precision of the comparison method

Duplicate measurements of each venous serum 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 5.

Table 3. Repeatability (CV) of the comparison method for CRP measured in venous serum samples.

Level	CRP interval mg/L	n*	Excluded results (statistical outliers)	Mean value CRP, mg/L	CV (90 % CI), %
1	0,42 – 19,59	106	0	4,6	1,8 (1,6 – 2,0)
2	20,14 – 53,52	42	0	36,0	1,3 (1,3 – 1,6)
3	60,08 – 166,36	23	0	97,5	1,3 (1,0 – 1,7)

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

Discussion
The CV for the comparison method was between 1,3 and 1,8 %.

6.2.3. The trueness of the comparison method

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

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

Date of survey	Assigned value, CRP mg/L (±15 % acceptance limits)	n	Mean Cobas 8000 CRP mg/L
2023-08-28	42,4 (36,0 – 48,8)	2	37,1
	69,9 (59,4 – 80,4)	2	60,9
2023-10-16	35,5 (30,2 – 40,8)	2	31,1
	62,8 (53,4 – 72,2)	2	57,5

Discussion

The trueness of the comparison method was confirmed by the results in the national EQA programme for CRP.

6.3. Analytical performance of LabPad Evolution Ksmart CRP achieved by intended users

The results below reflect the analytical performance of LabPad Evolution Ksmart CRP when used by the intended users; healthcare professionals, in PHCCs.

6.3.1. Internal analytical quality control

Seven results from the internal analytical quality control (Ksmart CRP + Controls, Biosynex SA), two levels, were outside the allowable control limits (data not shown). Six of them were repeated. Out of the repeated internal quality control samples, only one was still outside the allowable limits. The PHCC changed to a new test kit where the quality control was within the allowable limits. The test kit with two internal quality control results outside the allowable limits was not used during the evaluation.

One internal quality control result from PHCC3 (level 2, lot c) was considered a statistical outlier according to the criterion promoted by Burnett [7]. The result was not included in the calculation of the reproducibility of the internal analytical quality control.

The reproducibility (CV) achieved with the internal analytical quality control samples were 16,2 % for level 1 (n=76) and 16,3 % for level 2 (n=75). Raw data is attached for the requesting company only, attachment 6.

6.3.2. The precision of LabPad Evolution Ksmart CRP

Duplicate measurements of each capillary whole blood sample were performed on LabPad Evolution. 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 LabPad Evolution. Raw data is attached for the requesting company only, see attachment 7.

Table 5. Repeatability (CV) of LabPad Evolution for CRP measured in capillary whole blood samples. Results achieved by intended users in PHCCs.

Place	Level	CRP interval, mg/L	n*	Excluded results*** (statistical outliers)	Mean value CRP, mg/L	CV (90 % CI), %
PHCC1	Low	0,6 – 18,5	20	0	3,8	19,5 (15,5 – 26,8)
	Medium	20,0 – 56,5	8	0	32,6	27,2 (18,8 – 52,1)
	High	69,0 – 149,0	6**			
PHCC2	Low	0,9 – 11,0	21	0	4,9	16,7 (13,4 – 22,7)
	Medium	21,5 – 59,0	13	0	35,2	15,1 (11,4 – 22,8)
	High	62,0 – 169,0	7**			
PHCC3	Low	0,7 – 11,0	28	3***	4,2	26,6 (21,9 – 34,2)
	Medium	21,5 – 56,0	13	0	35,8	16,0 (12,1 – 24,2)
	High	74,5 – 109,0	4**			
PHCC4	Low	0,6 – 13,9	8	0	5,2	45,6 (32,2 – 82)
	Medium	28,0 – 50,5	8	0	38,3	19,0 (13,4 – 34,1)
	High	61,5 – 113,5	5**			
PHCC5	Low	0,7 – 9,1	23	1***	4,5	17,9 (14,4 – 23,9)
	Medium	24,0 – 58,0	7**			
	High		0			
PHCC All	Low	0,6 – 18,5	101	8***	4,4	24,9 (22,4 – 28,4)
	Medium	20,0 – 59,0	48	0	36,0	18,6 (15,9 – 22,5)
	High	61,5 – 169,0	22	0	101,9	21,5 (17,2 – 28,9)

* 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.
**n<8; CV not reported due to high degree of uncertainty.
*** ID 125, 236, 306, 317, 337, 405, 406 and 533 were statistical outliers according to Burnett's model [7] in the calculation of repeatability and therefore excluded.

Discussion

The CV achieved by intended users was between 18,6 and 24,9 % depending on the concentration level. Since the results, per concentration level, had overlapping CIs, the results from all five PHCCs were merged into CV all. The CV all was higher than the APS for all concentration levels.

Conclusion
When measurements were performed by the intended users the APS for repeatability (CV ≤10 %) was not fulfilled.

6.3.3. The bias of LabPad Evolution Ksmart CRP

The mean deviation (bias) of LabPad Evolution 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 attachment 5 and 7.

Table 6. Bias of LabPad Evolution for CRP measured in capillary whole blood. Results achieved by intended users in PHCCs.

	Level	n*	Excluded results (statistical outliers)	Mean value Comparison method, CRP, mg/L	Mean value LabPad Evolution, CRP, mg/L	Bias (95 % CI), mg/L	Bias, %
PHCC 1	1	21	0	4,5	5,0	0,50 (-0,05 – 1,05)	11,1
	2	4	0	35,0	37,4	2,35 (-6,59 – 11,29)	6,7
	3	8	0	114,9	107,5	-7,39 (-31,32 – 16,54)	-6,4
PHCC2	1	22	1**	4,1	5,2	1,15 (0,05 – 2,26)	28,3
	2	12	0	32,3	36,3	3,96 (0,74 – 7,17)	12,2
	3	7	0	110,2	119,2	8,97 (-1,6 – 19,53)	8,1
PHCC 3	1	29	0	3,7	3,9	0,20 (-0,02 – 0,42)	5,5
	2	13	0	39,2	39,9	0,66 (-4,70 – 6,02)	1,7
	3	3	0	99,6	95,3	-4,30 (-53,33 – 44,73)	-4,3
PHCC 4	1	6	0	2,8	2,7	-0,12 (-0,91 – 0,68)	-4,2
	2	8	0	38,2	38,3	0,07 (-5,47 – 5,61)	0,2
	3	5	0	91,5	87,6	-3,94 (-16,62 – 8,74)	-4,3
PHCC 5	1	23	1**	4,4	5,2	0,86 (-0,75 – 2,47)	19,6
	2	5	0	33,4	33,2	-0,17 (-3,60 – 3,28)	-0,5
	3	1	0	60,1	58,0	-2,08 (-0,75 – 2,47)	-3,5
PHCC All	1	100	6**	4,1	4,7	0,61 (0,17 – 1,05)	15,0
	2	42	0	36,0	37,5	1,55 (-0,50 – 3,60)	4,3
	3	24	1**	104,5	103,2	-1,29 (-9,56 – 6,97)	-1,2

* 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.
**SKUP ID 104, 115, 119, 205, 224, 242 and 501 were statistical outliers according to Burnett's model [7] in the calculation of bias and therefore excluded.

Discussion

The combined results from all five PHCCs shows a statistically significant positive bias between LabPad Evolution Ksmart CRP and the comparison method for level 1. For level 2 there was a positive bias between LabPad Evolution Ksmart CRP and the comparison method, and for level 3 a negative bias; these were not statistically significant.

6.3.4. The accuracy of LabPad Evolution Ksmart CRP

To evaluate the accuracy of CRP results on LabPad Evolution, the agreement between LabPad Evolution and the comparison method is illustrated in difference plots (figure 3 and 4). The first plot (figure 3a and b) shows the accuracy divided per PHCC and the second (figure 4a and b) per lot number of test kits. The limits for the allowable deviation according to the APS, are shown with stippled lines. All the first measurements from LabPad Evolution are included in the plots. The plots illustrates both random and systematic errors, reflecting the total measuring error in the LabPad evolution results. Raw data is attached for the requesting company only, see attachment 5 and 7.

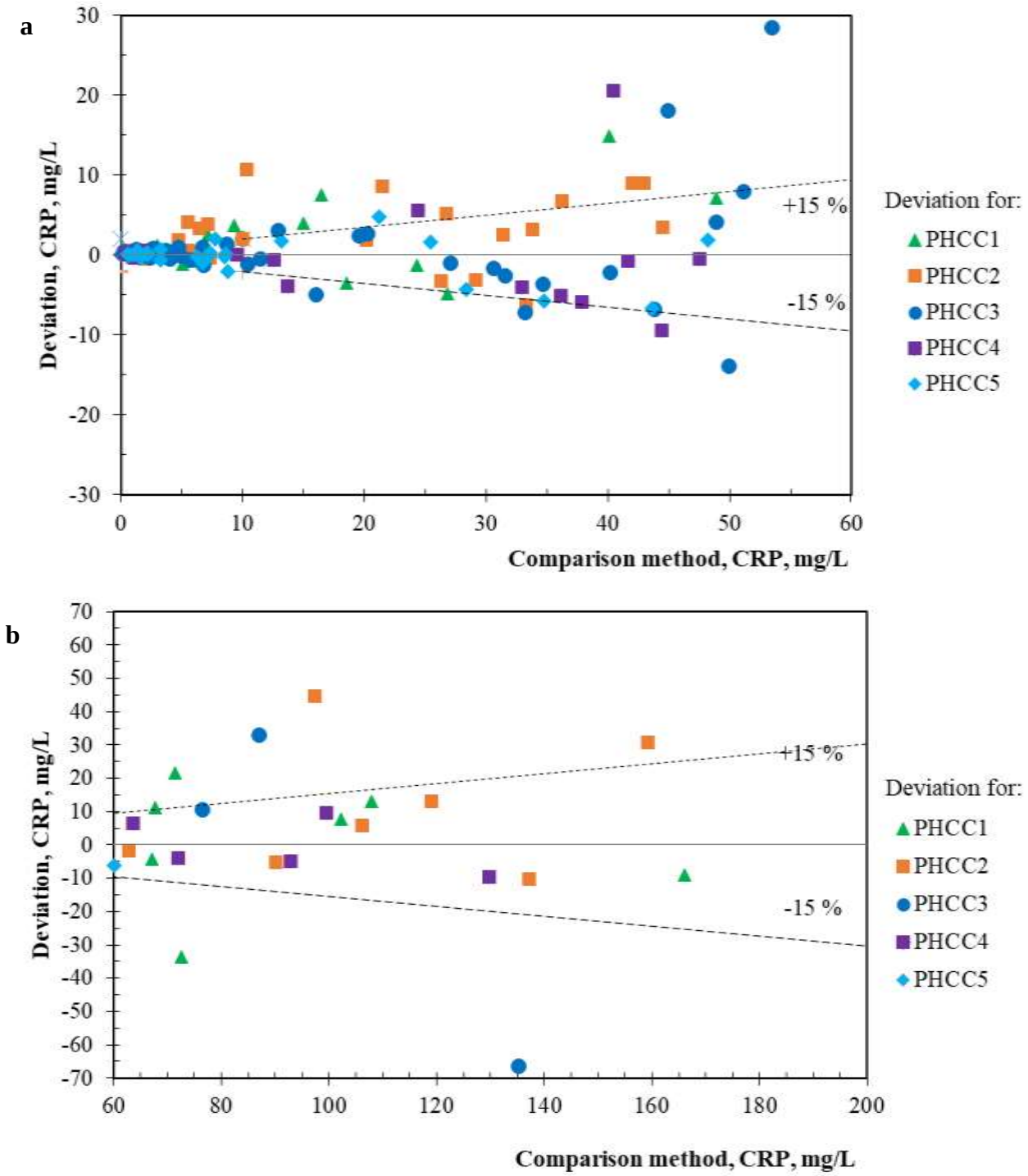

Figure 1. Accuracy of CRP results on LabPad Evolution achieved by intended users. Low and medium CRP results are shown in figure 3a and high CRP results in figure 3b. The x-axis represents the mean CRP result of the comparison method. The y-axis represents the CRP deviation in mg/L of the first capillary whole blood measurement on LabPad Evolution from the mean result of the corresponding sample of the comparison method. The different PHCCs are illustrated with different symbols; ▲ (PHCC1), ■ (PHCC2), ● (PHCC 3), ■ (PHCC 4), ♦ (PHCC 5). The stippled lines represent the allowable deviation limits of ≤±2,0 mg/L for CRP concentrations <10 mg/L and ≤±15 % for CRP concentrations ≥10 mg/L. Number of results (n) = 175. An account of the number of samples is given in section 6.1.

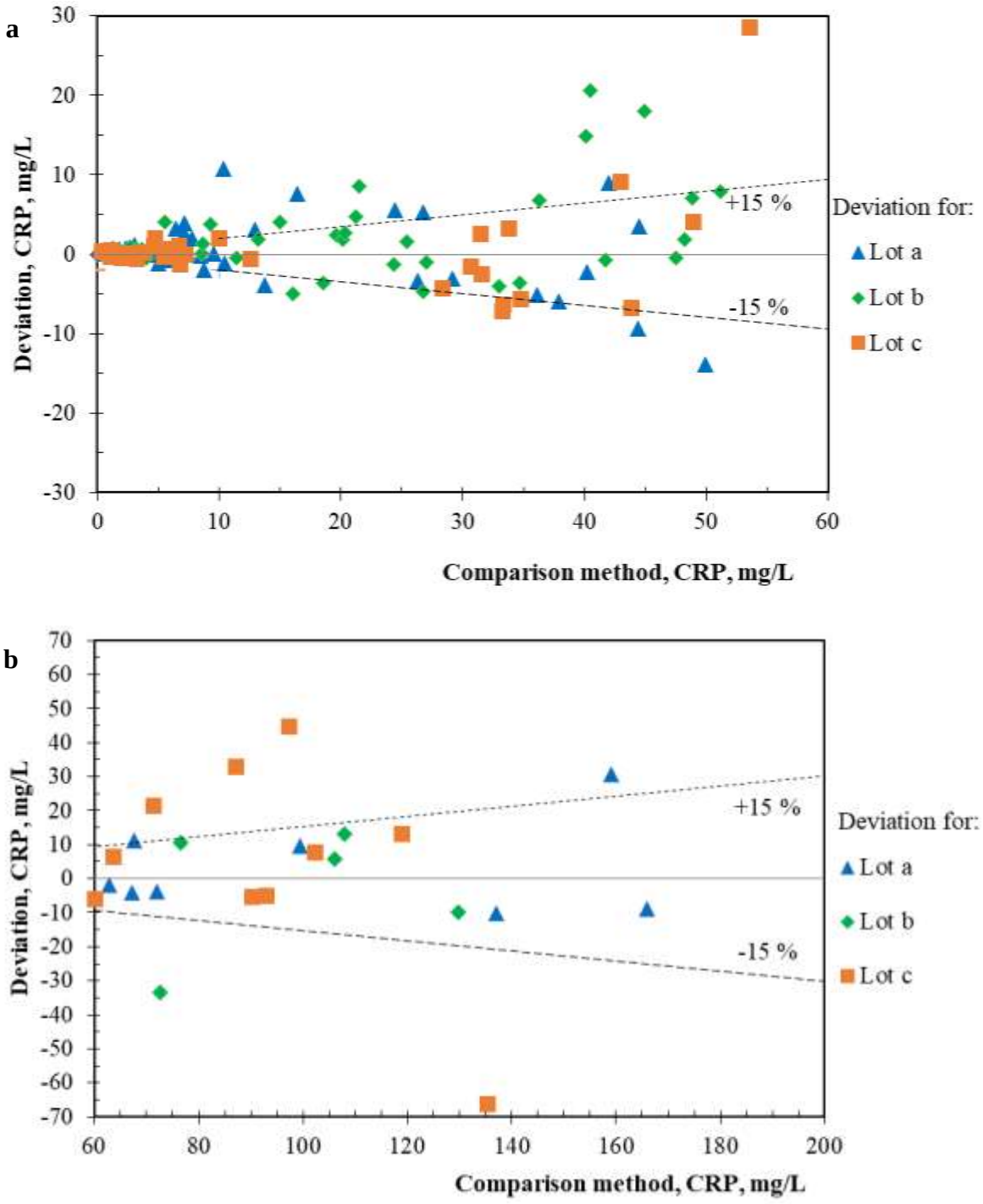

Figure 4. Accuracy of CRP results on LabPad Evolution achieved by intended users. Low and medium CRP results are shown in the upper plot and high CRP results in the lower plot presented per lot number. The x-axis represents the mean CRP result of the comparison method. The y-axis represents the CRP deviation in mg/L of the first capillary whole blood measurement on LabPad Evolution from the mean result of the corresponding sample of the comparison method. The different lots are illustrated with different symbols; ▲ (lot a), ♦ (lot b), ■ (lot c). The stippled lines represent the allowable deviation limits of ≤±2,0 mg/L for CRP concentrations <10 mg/L and ≤±15 % for CRP concentrations ≥10 mg/L. Number of results (n) = 175. An account of the number of samples is given in section 6.1.

Discussion
As shown in figure 3 and 4 the LabPad Evolution shows widely spread results, especially in a medium and high CRP concentration range. None of the lot numbers, nor any of the PHCCs in the evaluation stands out with a greater deviation than the others. Of 175 results, 141 var within the limits for allowable deviation of ±2,0 mg/L of the results of the comparison method for CRP concentrations <10 mg/L or within ±15 % for CRP concentrations ≥10 mg/L, corresponding to 80,6 % within the limits.

Conclusion
When measurements were performed by the intended users the APS for accuracy (≥95 % of the results within limits) was not fulfilled.

6.3.5. Reproducibility in heparin plasma

The reproducibility (CV) achieved with heparin plasma sample pools with approximate concentration of 10 mg/L and 100 mg/L were 25,0 % (mean 11,8 mg/L; range 7,7 – 20,0 mg/L; n=20) and 23,2 % (mean 106,3 mg/L; range 67,0 – 160,0 mg/L; n=20), respectively. Raw data is attached for the requesting company only, see attachment 8.

6.4. Evaluation of user-friendliness

6.4.1. Questionnaire to the evaluators

The most important response regarding user-friendliness comes from the intended users themselves. The end-users often emphasise 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 measuring system. SKUP has prepared detailed instructions for this.

The questionnaire is divided into four subareas:

Table A) Rating of ease of operation. Is the measuring system easy to handle?
Table B) Rating of the information in the manual / insert / quick guide
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. The rating of table C and the topics marked with grey colour in table A and B are based on information from the manufacturer.

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 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 on the user-friendliness of the measuring 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:
PHCC 1; two health secretaries.
PHCC 2; three health secretaries.
PHCC 3; three health secretaries.
PHCC 4; two health secretaries.
PHCC 5; one health secretary.

Table A. Rating of ease of operation

Topic	Rating	Rating	Rating	Rating	Option
To prepare the test / instrument	**S, S, S, S, S**	**Satisfactory**	Intermediate	Unsatisfactory	No opinion
To prepare the sample	**S, S, S, S, S**	**Satisfactory**	Intermediate	Unsatisfactory	No opinion
Application of specimen	**S, I[2], I[3], S, S**	**Satisfactory**	**Intermediate**	Unsatisfactory	No opinion
Specimen volume	**U[1], I[2], S, I[4], S**	**Satisfactory**	**Intermediate**	**Unsatisfactory**	No opinion
Number of procedure step	**S, U[2], U[3], S, S**	**Satisfactory**	Intermediate	**Unsatisfactory**	No opinion
Instrument / test design	**S, U[2], U[3], S, S**	**Satisfactory**	Intermediate	**Unsatisfactory**	No opinion
Reading of the test result	**E, E, E, E, E**	**Easy**	Intermediate	Difficult	No opinion
Sources of errors	**S, S, S, S, S**	**Satisfactory**	Intermediate	Unsatisfactory	No opinion
Cleaning / Maintenance	**S, N, N, S, S**	**Satisfactory**	Intermediate	Unsatisfactory	**No opinion**
Hygiene, when using the test	**S, I[1], U[3], S, S**	**Satisfactory**	**Intermediate**	**Unsatisfactory**	No opinion
Size and weight of LabPad Evolution	**S, S, S, S, S**	**Satisfactory**	Intermediate	Unsatisfactory	No opinion
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 or disposable**	+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 experienced personnel	Biomedical laboratory scientists	
Total rating by SKUP			**Intermediate**		

[1] Requires too much sample volume, especially if it should be used on children.
[2] Hard to fill the capillary tubes and to see when the capillary tubes are full. Risk of blood spilling when putting the capillary into the buffer tube. Time consuming procedure with many steps where you must use a timer. The design of the instrument was not good for left hand users.

[3)] Many steps before the sample can be analysed.
[4)] Too much volume to collect in the capillary.
[5)] Long time before a result was produced (combined preanalytical and analytical time). A holder for the capillary should be included, as it was hard to hold during sampling.

Additional positive comments:
The instrument is small and the time of measurement is short.
Simple and manageable instrument. The instrument took up little space.

Additional negative comments:
It’s easy to lose the “pearl” in the internal quality control. It’s hard to open the bottle for the low control.
Large differences between duplicate results.

Table B. Rating of the information in the insert and quick guide*

Topic	Rating	Rating	Rating	Rating	Option
Table of contents/Index	**S, S, N, S**	**Satisfactory**	Intermediate	Unsatisfactory	**No opinion**
Preparations/Pre-analytic procedure	**S, S, S, S**	**Satisfactory**	Intermediate	Unsatisfactory	No opinion
Specimen collection	**S, S, S, S**	**Satisfactory**	Intermediate	Unsatisfactory	No opinion
Measurement procedure	**S, S, S, S**	**Satisfactory**	Intermediate	Unsatisfactory	No opinion
Reading of result	**S, S, S, S**	**Satisfactory**	Intermediate	Unsatisfactory	No opinion
Description of the sources of error	**S, S, S, S**	**Satisfactory**	Intermediate	Unsatisfactory	No opinion
Help for troubleshooting	**S, S, N, S**	**Satisfactory**	Intermediate	Unsatisfactory	**No opinion**
Readability / Clarity of presentation	**S, S, S, S**	**Satisfactory**	Intermediate	Unsatisfactory	No opinion
General impression	**S, S, S, S**	**Satisfactory**	Intermediate	Unsatisfactory	No opinion
Measurement principle	**S**	**Satisfactory**	Intermediate	Unsatisfactory	
Available insert in Danish, Norwegian, Swedish	**S**	**Satisfactory**	Intermediate	Unsatisfactory	
Total rating by SKUP		**Satisfactory**			

** The ratings from one PHCC was excluded due to intermediate response on all topics in table B without any explanation.*

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

Topic	Rating	Rating	Rating
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 day or disposable**	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[1]**
Total rating by SKUP	**Satisfactory**		

[1)] When the control "pearl" is solved in the buffer the quality control has a stability of 1 day.

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

Topic	Rating	Rating	Rating
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**		

6.4.2. Assessment of the user-friendliness

Assessment of the ease of operation (table A)
The ease of operation was in total assessed as intermediate, as there were several intermediate and unsatisfactory ratings on vital steps of the handling procedure. The motivation for the negative ratings were most regarding big sample volume, difficulties in using the capillary tube and time-consuming steps before the sample could be analysed.

Assessment of the information in the manual (table B)
The quick guide and package insert were in total assessed as satisfactory.

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

Assessment of analytical quality control (table D)
The analytical quality control was in total assessed as satisfactory. The usefulness of the internal quality control was assessed as intermediate due to considerably large imprecision in the internal analytical quality control material from the manufacturer, which is not optimal for revealing failing analytical quality. The reading of internal quality control and external quality control were assessed as satisfactory.

Conclusion
The ease of operation for LabPad Evolution Ksmart CRP was rated as intermediate, while the information in the manual, time factors and analytical quality control possibilities were rated as satisfactory. In total, the user-friendliness of LabPad Evolution Ksmart CRP was rated as intermediate, due to intermediate and/or unsatisfactory ratings on vital steps of the handling procedure. The performance specification for user-friendliness was not fulfilled.

7. References

1. Christensen NG., Monsen G. & Sandberg S. Utprøving av analyseinstrumenter, 1997. Alma Mater Forlag ISBN 82-419-0230-1.

2. Sandberg S. *et al.* Defining analytical performance specifications: consensus statement from the 1st Strategic Conference of the European Federation of Clinical Chemistry and Laboratory Medicine, Clin Chem Lab Med 2015; **53**:833 – 835.

3. Ceriotti F. *et al*. Criteria for assigning laboratory measurands to models for analytical performance specifications defined in the 1st EFLM Strategic Conference. Clin Chem Lab Med 2017; **55** (2):189 – 194.

4. Kvalitetssikring og kvalitetskrav til laboratoriemedicinske aktiviteter i almen praksis. Udarbejdet af Regionernes Lønnings- og Takstnævn (RTLN) og Praktiserende Lægers Organisation (PLO). 2010. https://www.laeger.dk/sites/default/files/kvalitetssikring_og_kvalitetskrav_til_laboratoriemedicinske_aktiviteter_i_almen_praksis_2010.pdf (in Danish, accessed, 2024-01-12)

5. Commission of the European Communities. EUR 23756 EN – Joint Research Centre – Institute for Reference Materials and Measurements. Zegers I. *et al.* Certification of C-reactive protein in reference material ERM-DA472/IFCC. 2011.

6. The IFCC – IUPAC terminology for properties and units. http://www.ifcc.org/ifcc-scientific-division/sd-committees/c-npu/npusearch/ (accessed 2024-01-12)

7. Burnett RW. Accurate estimation of standard deviations for quantitative methods used in clinical chemistry. Clin Chem 1975; **21** (13): 1935 – 1938.

Attachments

1. Facts about LabPad Evolution Ksmart CRP
2. Information about manufacturer, retailers and marketing
3. Product specifications for this evaluation, LabPad Evolution
4. Statistical expressions and calculations
5. Raw data, CRP results from the comparison method
6. Raw data, internal analytical quality control results, LabPad Evolution Ksmart CRP, intended users
7. Raw data, LabPad Evolution CRP results, intended users
8. Raw data, LabPad Evolution CRP results, reproducibility study
9. Comments from Biosynex Nordic A/S

Attachments with raw data are included only in the copy to Biosynex Nordic A/S.

Facts about LabPad Evolution Ksmart CRP

This form is filled in by Biosynex Nordic A/S.

Table 1. Basic facts

Name of the measuring system:	LabPad Evolution and Ksmart CRP
Dimensions and weight:	L: 17,2 cm W: 7,4 cm H: from 2,0 to 4,6 cm
Components of the measuring system:	LabPad Evolution: Point of care reader Ksmart CRP: CRP test
Measurand:	CRP
Sample material:	Capillary whole blood, venous whole blood, plasma
Sample volume:	10µL whole blood, 6µL plasma
Measuring principle:	Lateral flow with fluorescence detection (europium)
Traceability:	International CRP standard from BBI solutions
Calibration:	Automatic in the Datamatrix read by the LabPad at the start of the test
Measuring range:	0,5 – 200 mg/L
Haematocrit range:	30%-50%
Measurement time:	3 minutes; 1 minute for sample migration, 2 minutes in the LabPad
Operating conditions:	15-30°C
Electrical power supply:	For the LabPad on battery
Recommended regular maintenance:	No maintenance
Package contents:	• The LabPad® Evolution reader • A Charger with a main unit and a micro USB-B cable • A Carrying case • The User manual
Necessary equipment not included in the package:	Lancet gauge 21 for the capillary whole blood sample

Table 2. Post analytical traceability

Is input of patient identification possible?	Yes
Is input of operator identification possible?	Yes
Can the instrument be connected to a bar-code reader?	Yes
Can the instrument be connected to a printer?	No
What can be printed?	NA
Can the instrument be connected to a PC?	Yes
Can the instrument communicate with LIS (Laboratory Information System)? If yes, is the communication bidirectional?	The LabPad Evolution can communicate bidirectionally
What is the storage capacity of the instrument and what is stored in the instrument?	1000 tests and QC results, Operator ID, Patient ID,…
Is it possible to trace/search for measurement results?	No

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

Name of the reagent/test strips/test cassettes:	Ksmart CRP
Stability in unopened sealed vial:	18 months
Stability in opened vial:	2 hours
Package contents:	Ksmart® CRP tests in individual pouches with desiccant: x25 -Buffer tubes: x25 -End-to-end capillary pipettes: x25 (for capillary whole blood only) -Instructions for use: x1

Table 4. Quality control

Electronic self check:	Yes
Recommended control materials and volume:	1040012_C
Stability in unopened sealed vial:	Stability of the kit: lyophilized CRP control bead
Stability in opened vial:	Use immediately after reconstitution in pre-filled buffer
Package contents:	25 Ksmart® CRP tests in individual pouches with desiccant - 25 pre-filled buffer tubes - 25 end-to-end capillary pipettes (for capillary whole blood only) - 4 lyophilized CRP control beads in individual pouches with desiccant (“Control Bead Ksmart® CRP) - 2 pre-filled bottles with white caps for “Low” level CRP control reconstitution - 2 pre-filled bottles with black caps for “High” level CRP control reconstitution (“Ksmart® CRP Control High”) - 1 “Quality Control Card” - 1 set of instructions for use

Information about manufacturer, retailers and marketing

This form is filled in by Biosynex Nordic A/S

Table 1. Marketing information

Manufacturer:	Biosynex SA
Retailers in Scandinavia:	Denmark: Biosynex Nordic A/S Norway: Biosynex Nordic A/S Sweden: Biosynex Nordic A/S
In which countries is the system marketed:	Globally ☐ Scandinavia ☒ Europe ☒
Date for start of marketing the system in Scandinavia:	14/11/2022
Date for CE-marking:	24/05/2022
In which Scandinavian languages is the manual available:	Denmark, Sweden, Norwegian, Finland.

Product specifications for this evaluation, LabPad Evolution Ksmart CRP

LabPad Evolution instrument serial numbers

Serial no.	Used by
1366049000029	PHCC1
1366049000014	PHCC2
1366049000021	PHCC3
1365523000255	PHCC4
1365523000259*	PHCC5
1365523000259*	Hospital laboratory

*The same instrument was used first for the reproducibility study at the hospital laboratory, and then at PHCC5.

Ksmart CRP test kits

Lot no.	Alias	Expiry date	Used by
00003A	Lot a	2025-04-12	All evaluation sites
00004A	Lot b	2025-04-19	
00005A	Lot c	2025-04-26	

Ksmart CRP internal analytical quality control kit (Ksmart CRP + Controls)

Control	Lot no	Expiry date	Used by
Control Low	CRPL230606	2025-07-20	All evaluation sites
Control High	CRPH230606	2025-07-20	

Target values for Ksmart CRP + Controls*

	Control Low, CRP mg/L		Control High, CRP mg/L	
	Target	**Allowable range**	**Target**	**Allowable range**
Lot a	14,8	9,3 – 20,3	74,0	45,3 – 102,6
Lot b	13,6	9,1 – 18,2	73,5	51,0 – 96,0
Lot c	13,9	8,8 – 19,0	62,9	42,7-83,2

*Target values are dependent on lot number for test kit.

Other equipment used in the evaluation

Other Equipment	Lot no	Expiry date	Used by
BD Vacutainer 5mL, Becton Dickinson	3058372	2024-08-24	All evaluation sites
Accu-Chek Safe-T Pro Plus*			All evaluation sites

*Lot no. and expiry date unknown

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]:

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

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. 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.

b. Burnett RW. Accurate estimation of standard deviations for quantitative methods used in clinical chemistry. *Clin Chem* 1975; **21** (13): 1935 – 1938.
c. Dahlberg G. Statistical methods for medical and biological students, 1940. Chapter 12, Errors of estimation. George Allen & Unwin Ltd.
d. 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.
e. Fraser C.G. Biological variation: From principles to practice, 2006. Chapter 1, The Nature of Biological Variation. AACC Press ISBN 1-890883-49-2.

Raw data, CRP results from the comparison method

Shown to the requesting company only.

Raw data, internal analytical quality control results, LabPad Evolution Ksmart CRP, intended users

Shown to the requesting company only.

Raw data, LabPad Evolution CRP results, intended users

Shown to the requesting company only.

Raw data, LabPad Evolution CRP results, reproducibility study

Shown to the requesting company only.

Comments from Biosynex Nordic A/S

Attachment (Attached Letter)

to the SKUP/2024/136 report by Biosynex Nordic A/S
15.03.2024

The aim of the present SKUP evaluation regarding LabPad Evolution Ksmart CRP (in short: LabPad CRP) was to assess its analytical performance and user-friendliness as a Point-of-Care devise used by primary health care professionals. Thus, the correlation curve between LabPad CRP and CRP measured at the Department of medical biochemistry and pharmacology, Haukeland University Hospital, Norway using cobas 8000, c 702 (Roche) is of great importance and showed an excellent lineary correlation between LabPad CRP and cobas 8000 (Figure 1).

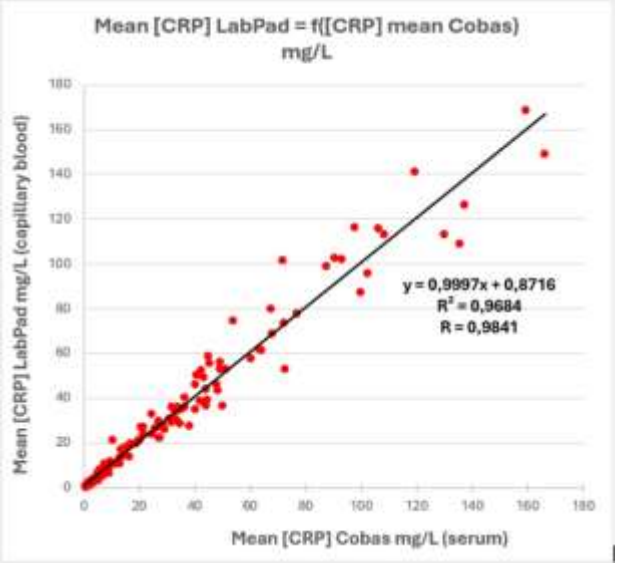

Figure 1. The correlation between mean LabPad CRP versus mean CRP measurement by cobas 8000, c 702 (Roche) based on included values in the SKUP/2024/136 evaluation.

Moreover, in Figure 1 the thresholds of CRP at 10 mg/L and 100 mg/L revealed that LabPad CRP was in concordant with the routine method at 10 mg/L and 100 mg/L and that outliers were close to these.

Although, the present SKUP evaluation revealed a bias of -6.4 to +28.3% regarding LabPad CRP, a bias of 28.3% entails that CRP measured by LabPad is 5.2 mg/L compared to 4.1 mg/L by the comparison methods. Likewise, a bias of -6.4% entails that LabPad CRP was 107.5 mg/L compared to 114.9 mg/L by the comparison methods. Thus, a bias of LabPad CRP was without impact. The main conclusion is therefore that LabPad CRP in a Point-of-Care setting is qualified to rubricates / triages completely satisfactory.

Regarding the user-friendliness of the LabPad CRP it was found only for the ease of operation as intermediate, while the information in the manual, time factors and analytical quality control possibilities were all rated as satisfactory. However, it should be noted that Biosynex Nordic A/S

doesn’t provide only “a product”, but “a Point-of-Care solution” including 1) introduction, 2) training and 3) close follow-up during the implementation and running faces. However, our normal procedure included close follow-up during the implementation and running faces was not allowed during the SKUP evaluation but could most likely had raise the ease of operation of the devise.

Finaly, as the LabPad CRP is a new product on the market, Biosynex Nordic A/S continues to improve the product development. The feedback of the present SKUP report regarding the user-friendliness is already implemented as the number of steps during sample preparation has been decreased combined with improved management of the quality controls.