i-CHROMA

A system for measurement of P—C-reactive protein
manufactured by Boditech Med Inc.

Report from an evaluation
under standardised and optimal conditions
and in primary health care
organised by SKUP

Evaluated at the request of Medic24, Norway

SKUP/2011/90

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The report was written by SKUP, 2010-2011.
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The organisation of SKUP

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

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

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

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

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

SKUP reports are published at www.skup.nu. In addition, SKUP reports are published at www.skup.dk, where they are rated according to the national Danish quality demands for near patient instruments used in primary health care. SKUP as an organisation has no responsibility for www.skup.dk.

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

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

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

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A detailed list of previous SKUP evaluations is included in the attachments.
Attachments with raw data are only included in the copy to Medic24.

1. Summary

Background
The *i*-CHROMA™ CRP test was evaluated by SKUP in 2008. Due to several product changes, SKUP performed a new evaluation of *i*-CHROMA™ CRP in 2009. In this second evaluation, the analytical quality goal for accuracy was not fulfilled with venous whole blood samples. With plasma samples the quality goal was fulfilled, despite a bias of -16,5%. The user-friendliness was assessed as satisfying. As a consequence of the results achieved in this second evaluation, the manufacturer adjusted the calibration of the method, and Medic24 applied for a third evaluation of the *i*-CHROMA system in 2010.

The aim of the evaluation
- To examine the imprecision of *i*-CHROMA achieved with whole blood samples, at least100 venous and at least100 capillary patient samples in a hospital laboratory
- To examine if the instrument measures equally correct at both low and high P—CRP concentrations.
- To compare the instrument with an established hospital laboratory method for P—CRP
- To examine the imprecision achieved with 40 patient samples in each of two primary health care centres
- To evaluate the of user-friendliness of *i*-CHROMA in hospital laboratory and primary health care centres
- To examine the influence of hematocrit on the results from i-Chroma
- To evaluate the Medic24 control material

Materials and methods
Bias and repeatability of *i*-CHROMA were calculated from duplicate results. Venous whole blood samples and capillary samples from 100 individuals were examined in the hospital, and capillary samples from 80 patients were tested in primary health care centres. The selected comparison method was a Cobas Integra C-Reactive Protein (Latex) method from Roche, using serum as sample material. This immunoturbidi-metric method was operated according to the instructions from Roche using reagents, instrument, and calibrators from Roche. The results were adjusted with a factor (0,943) to be aligned with the Certified Reference Material (CRM) 470.

Results
114 samples (mean 54,8 mg/L, range 1,0-264 mg/L) were measured using four lots of *i*-CHROMA test strips. The results were compared to duplicate results from the comparison method. In the hospital evaluation, >95% of the *i*-CHROMA whole blood sample results, both capillary and venous, were within ±26% from the comparison method results. The bias was less than ±10% in all three concentration levels and the repeatability (CV) was 4,3% for capillary samples and 3,9% for venous samples. In the primary health care evaluation, only capillary samples were analysed in duplicates. In one primary health care centre the repeatability was 5,7% whereas it was 15,0% in the other. This means that the quality goal of <10% was fulfilled only in one of the primary health care centres. According to two of the evaluators the instrument is best suited for users with laboratory experience. The reproducibility achieved with control material was 3,1% in the hospital evaluation and 16% and 20% in the two primary health care centres, respectively.

Conclusion
In the hospital laboratory evaluation the analytical quality goals were fulfilled with both capillary and venous whole blood samples. One primary health care centre achieved the goal for repeatability while the other did not. The CV was 5,7% and 15%, respectively. Two of the evaluators mentioned, that the instrument might have some pitfalls for un-skilled users.

Comments from Medic24
A letter (attachment 8) with comments from Medic24 is attached to the report

2. Quality goals

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

2.1. Analytical quality goals

International guidelines for analytical quality requirements for Plasma—C-reactive protein (P—CRP) are few. The biological within-subject-variation is 42,2% and the biological between-subject-variation is 76,3% for healthy individuals [1]. The reference interval is <3 mg/L. The desirable quality specifications [2-6] calculated from the biological variation give high figures; imprecision <21,1% CV, bias ±21,8%, and total error <56,6%. As the CRP test is mostly used for non-healthy individuals with higher CRP-concentrations, narrower quality limits are justified as proposed below by SKUP for the present evaluation. In Denmark, the P—CRP analyses used in primary health care and in hospital laboratories have different requirements to quality [7]. Norway and Sweden have no similar requirements.

SKUP:
In SKUP, the analytical quality goal for P—CRP is:

Allowable deviation $\leq \pm [\,|\,\text{bias}\,|\, + 1{,}65 \times \text{CV}]$, where bias <10% and CV <10%
$= 10 + 1{,}65 \times 10 \sim \leq \pm 26\%$

In Denmark:

In Denmark the analytical quality goals are:

For P—CRP >15 mg/L:

Near Patient Tests used in primary health care:	Bias ≤±10% and imprecision ≤10%
Hospital laboratory methods, used as comparison methods:	Bias ≤±3% and imprecision ≤5%

2.2. Quality goals for user-friendliness

The user-friendliness of the tested equipment is separated in four sub-areas in the questionnaire:

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

Evaluation of user-friendliness is graded as satisfactory, intermediate or unsatisfactory, also depicted by the colours green, yellow, and red.

2.3. SKUP's quality goals for the present evaluation

Based on the discussion about quality goals above, SKUP has decided to assess the results from the evaluation of the *i*-CHROMA CRP system against the quality goals in table 1.

Table 1. Quality goals in the evaluation of the *i*-CHROMA CRP system

	Goal
Imprecision (CV)	≤10%
Inaccuracy (allowable deviation)	≤±26%
Fraction of technical errors	≤2%
User-friendliness	satisfactory

3. Materials and methods

3.1. Definition of P—CRP

The Scientific Division of IFCC (International Federation of Clinical Chemistry and Laboratory Medicine) and IUPAC (International Union of Pure and Applied Chemistry) work in a joint committee C-NPU (Committee of Nomenclature, Properties, and Units). The committee has described what is measured in diagnostic tests. The descriptions are listed in the ”NPU database” [8]. In the database, the recommended name is given for the measurand and with which unit the result should be reported. In the NPU-database, the C-reactive protein-measurements in this evaluation are described as:

Table 2. Name and codes for the CRP test according to C-NPU

NPU code	Full name of test according to NPU	Commonly used short name	Unit
NPU19748	Plasma—C-reactive protein; mass concentration . = ?	P—CRP	mg/L

The *i*-CHROMA CRP system usually makes measurements on whole blood but the results are expressed as the corresponding plasma concentrations of CRP. The measured *i*-CHROMA whole blood sample results are automatically converted to plasma results assuming that the hematocrit (EVF) for all samples is 0,40.

There is no separate NPU code for measurements of P—CRP using near patient instrument analysing on capillary blood.

3.2. Traceability for P—CRP results

All P—CRP tests should produce results that are traceable to a C-reactive protein (CRP) reference material. The results in this evaluation are traceable to the Certified Reference Material (CRM) 470 [9] that was analysed using the comparison method after the evaluation.

3.3. The *i*-CHROMA device

The manufacturer primarily delivered the following information regarding the *i*-CHROMA CRP system.

3.3.1. *Description of the i-CHROMA*

The *i*-CHROMA CRP Test system [10-13] is a small near-patient system intended for use by health care personnel in primary health care centres, hospital clinics, etc. *i*-CHROMA can be used either as a basic system where the user manually records the results, or a printer can be purchased to print the results.

The *i*-CHROMA CRP Test system consists of four parts: A capillary blood collector, a detector buffer, a disposable CRP strip, an *i*-CHROMA reader, and a System Control strip to test the *i*-CHROMA reader for malfunctions.

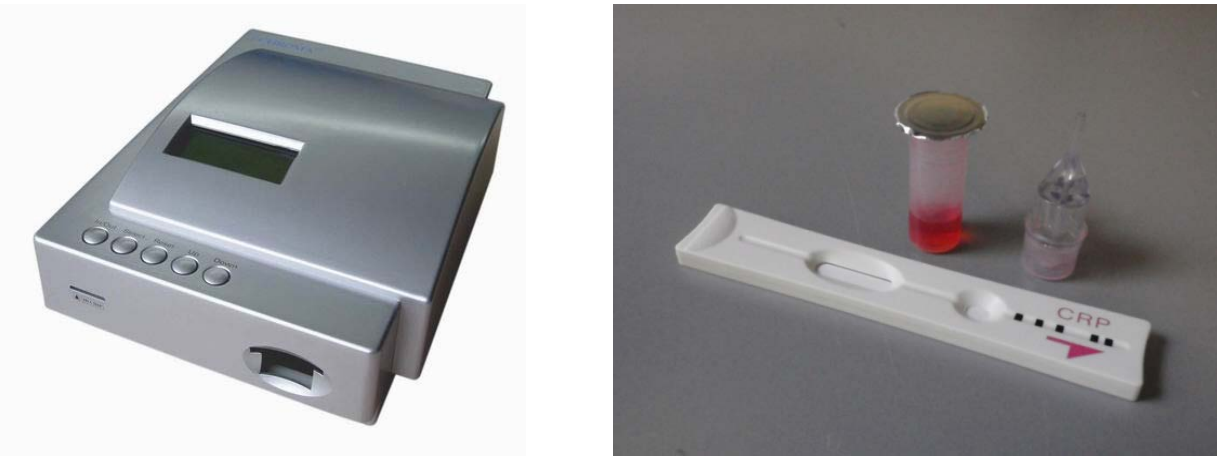

Figure 1. Picture of the *i*-CHROMA reader and a picture of the test strip, capillary blood collector, and buffer.

Capillary whole blood, venous EDTA-blood, and serum may be analysed on the *i*-CHROMA and the sample size is 10 µL. The measuring range is 2,5 – 300 mg/L and the test result is displayed after approximately three minutes. The *i*-CHROMA instrument does not adjust for the actual hematocrit in the samples. The hematocrit is assumed to be 0,40 in all samples.

Each lot of test strips is supplied with a unique calibration chip, which provides *i*-CHROMA with lot specific calibration data. When changing lot the user has to change the chip inserted in *i*-CHROMA containing the calibration data. Whenever a test strip is inserted, *i*-CHROMA checks that the barcode on the strip is identical to the calibration chip inserted. If this is not the case, an error will occur. A calibration chip is supplied with each box of test strips.

When turning on the *i*-CHROMA instrument it performs an automatic self-test. A System Check Cartridge is also provided to be used whenever lot numbers are changed. This cartridge automatically scans for optical and/or mechanical errors. Running a System Check Cartridge is done in the same way as the last step of a normal test procedure.

The *i*-CHROMA test strips are packed individually in foil and can be stored at room temperature until they expire. When unpacked, they must be used within ten minutes. The buffer cups can be kept at +4 ^{o}C until they expire, but can be kept for up to two weeks at room temperature. They must reach room temperature before sampling and therefore must be taken out of the refrigerator at least ten minutes before sampling.

Processing a sample should be initiated immediately after the capillary puncture and all steps of the procedure should be done continuously hereafter.

Analysing a patient sample
A short version of the procedure for analyzing capillary blood on *i*-CHROMA is shown below in figure 2. The illustrations and explanations were found in the Medic24 Quick reference guide. Venous samples can be analyzed as well, either as serum or as EDTA-blood.

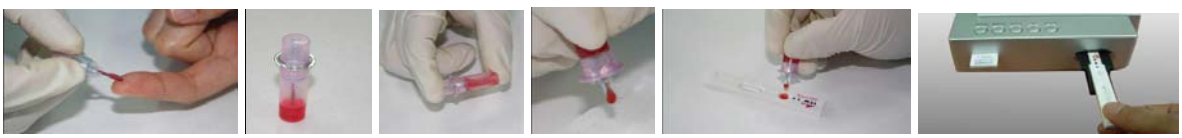

Figure 2: Analysing a patient sample. Please see attachment 2 for a full guide to sampling (Danish).

- Capillary blood is drawn from a fingertip and 10 µL is collected with the capillary blood collector. It is important that no blood come on the outside of the collector. If this is the case, the blood must be wiped away e.g. with a piece of paper
- Squeezing the buffer cup, the capillary sample is placed in the buffer cup through the already perforated foil
- The sample is mixed by turning it ten times
- The first two drops of blood/buffer mix is discarded
- Two drops of blood/buffer mix are dripped on the test strip in the designated window
- The test strip is placed in the reader. After pressing the select button, the procedure is automatic and the result is displayed on-screen after three minutes

3.3.2. *Analytical principle*

The *i*-CHROMA CRP test is used for measuring the concentration of P—CRP in human blood, serum, and EDTA-plasma. For measurement of the P—CRP concentration, a sandwich immunochromatography technology is used. 10 µL of whole blood is mixed with 500 µL of detector buffer containing fluorescence labelled anti-CRPmAb and anti-rabbit-IgG. The mixture is loaded onto the well of a test strip and as the test strip is inserted in the *i*-CHROMA reader, the complex-bound CRP migrates the along the nitrocellulose matrix. The CRP-complex is immobilised on the matrix by anti-CRP bound to the matrix and after three minutes of immune reaction, the test and the control lines are scanned for fluorescence intensity. The fluorescence intensity is converted into a P—CRP concentration calculated by a pre-programmed calibration process. The result of the test is displayed on the reader as mg/L. If the optional printer is connected, a printout is automatically made. The principle of the fluorescence detection and calculation of the analyte concentration is shown in figure 3.

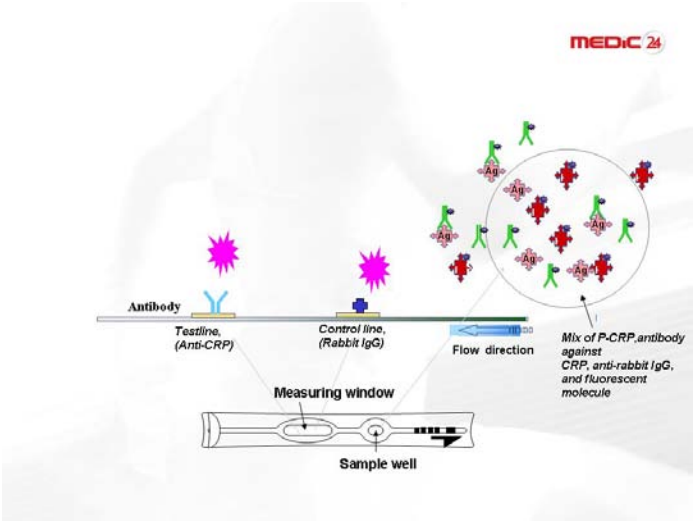

Figure 3: The figure shows the principle of the fluorescence detection and calculation of the analyte concentration (drawing supplied by Medic24)

3.3.3. *Product information, i-CHROMA*

Boditech Med Inc in Korea manufactures the *i*-CHROMA.
Technical data from Boditech Med Inc is shown in table 3. For more details about the *i*-CHROMA, see attachment 1.

Table 3. Technical data from Boditech Med Inc

Technical data for *i*-CHROMA	
Optimal operating temperature	+15 to +35^{o}C
Humidity	maximum 75%
Sample material	capillary blood, venous whole blood, serum, or plasma
Sample volume	10 µL
Measuring time	3 minutes
Measuring range	2,5 to 300 mg/L
Hematocrit	Not adjusted (0,40 assumed for all samples)
Storage capacity	100 results
Electrical power supply	AC (100-240V)
Operating time with battery	— (no battery)
Dimensions	width 18,5 cm; depth 25 cm; height 8 cm
Weight	1,2 kg

The following instruments and reagents were used in the evaluation:

i-CHROMA readers	Four units:	
	PFR09K271872 (instrument 1)	
	PFR09K271897 (instrument 2)	
	PFR09K271871 (instrument 3)	
	PFR09K271897 (instrument 4) back-up instrument	
System Check Strips	PFR09K271871 expiration date: May 2011	
	PFR09K271860 expiration date: May 2011	
Printers	D272G1AA900020	
	D272G1AA900018	
	D272G1AA900032	
Test Strips and buffers	WFC1A03 (lot 3)	expiration date: 2010.05.25
	WFE1A04 (lot 4)	expiration date: 2010.07.25
	WFH1A05 (lot 5)	expiration date: 2010.10.25
	WFL6A10 (lot 10)	expiration date: 2011.08.01
Controls	RCGA03	expiration date: 2011.03

3.3.4. *Manufacturer of i-CHROMA*

BodiTech Med. Inc.
1144-2, Geodu-ri
Dongnae-Myon
Chuncheon
Kangwon-Do, Korea
Phone: (+82) 33-243-1400
Fax: (+82) 33-243-9373
www.boditech.co.kr

Contact person within Boditech Med Inc:
Joung Dae Moon
mail: moonjd@boditech.co.kr

3.3.5. *Suppliers in the Scandinavian countries*

Denmark and Norway:

Hagebyvegen 40
3734 Skien
Norway
Phone: +47 35570300
Fax: +47 35570301
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Phone: + 46 33 23 00 99
Fax: + 46 33 23 00 28
E-mail: kundservice@medic24.se
www.medic24.se

3.4. The selected comparison method

The standard protocol for evaluations organised by SKUP includes a comparison of the results of the evaluated measurement system with the results from a well-established hospital method. The hospital method used in this evaluation of *i*-CHROMA is the routine method at the Department of Clinical Biochemistry at Hillerød Hospital. Hereafter called "the comparison method".

3.4.1. *The comparison method in this evaluation*

The following information regarding the comparison method is taken primarily from Roche.

Instrument:	Roche Cobas Integra 800. Four instruments were used during the evaluation, called Integra 1a and 1b (Integra 1a was replaced with Integra 1b on the 5th of July during the evaluation), 2, and 3. Integra 3 was used as a back-up instrument for the other instruments.
Reagent:	C-Reactive Protein (Latex) from Roche (CRPLX)[14]
Traceability:	Certified Reference Material (CRM) 470 [9]
Samples:	Venous serum, collected in tubes containing gel separator see section 3.4.6.
Calibration:	A six point calibration using C.f.a.s. (Calibrator for automated systems) protein from Roche
Measurement Principle:	The CRPLX is a particle enhanced turbimetric assay, where human CRP agglutinates with latex particles coated with monoclonal anti-CRP antibodies. The concentration of the precipitate is determined turbimetrically at 552 nm.

3.4.2. *Verification of the analytical quality of the comparison method*

After the evaluation was complete, the comparison method was checked with the CRM 470, on two separate days. The bias was calculated as the deviation of the mean of nine measurements (two instruments) from the calculated concentrations of the CRM 470.

External quality control: Labquality, Finland: The clinical biochemical department at Hillerød Hospital participates in the Labquality survey number 1072 once a month. Labquality originates in Finland and the control samples are distributed in Denmark via DEKS (Dansk Institut for Ekstern Kvalitetssikring for Laboratorier i Sundhedssektoren)

Internal quality control: Two control materials from DEKS were analysed every day:
HK02 High CRP
HK10 Special or HK06
The control material HK02 High CRP from DEKS is analysed every day as a normal sample. The mean concentration of HK02 High CRP is reported to DEKS once a month.
In addition the control material Precipath Protein from Roche, were analysed once a day.

3.4.3. *Product information, the comparison method*

Instruments: Roche Cobas Integra 800
Serial numbers: CL395743, CL396447, CL397084, and CL396594
For measurements of hematocrit two Sysmex XE-5000 instruments were used: serial numbers A1780 and A1765.

Reagent: CRPLX:
lot number 619676, expiration date Sept 9th, 2011
lot number 624554, expiration date Dec 12th, 2011
lot number 614798, expiration date May 5th, 2011

Calibrators: C.f.a.s. Protein:
lot number 153529, expiration date April 30th, 2011
lot number 155449, expiration date Oct 30th, 2011
Calibrations were made on the following dates:
Integra 1: April 26th and 29th 2010, June 2nd 2010, Aug 29th 2010
Integra 2: April 26th and 29th 2010, June 11th, 2010, Sept 9th 2010
Integra 3: March 3rd 2010, May 11th 2010, Sept 9th 2010

Internal quality control: Precipath Protein:
lot number 153527, expiration date: April 4th, 2011
lot number 154789, expiration date: Aug.8th, 2011

3.4.4. *Procedures at the laboratory*

The venous samples for the comparison method were analysed as routine samples. However, the samples were analysed in duplicates on two different instruments, and this is a deviation from the normal routine procedure. Integra 1a, 1b, and 2 were primarily used in the evaluation, with Integra 3 as a back up in case of problems with either of the two main instruments.

3.5. Planning of the evaluation

3.5.1. *Background for the evaluation*

i-CHROMA reader with CRP test strips is a P—CRP system designed for capillary blood testing performed by health care professionals. The *i*-CHROMA system is produced by Boditech Med Inc. and is in Scandinavia supplied by Medic24. *i*-CHROMA was evaluated by SKUP in 2008 for the first time. Due to several product changes, SKUP performed a new evaluation of *i*-CHROMA™ CRP in 2009. In this second evaluation, the analytical quality goal for accuracy was not fulfilled with venous whole blood samples. With plasma samples the quality goal was fulfilled, despite a bias of -16,5%. The user-friendliness was assessed as satisfying. As a consequence of the results achieved in this second evaluation, the manufacturer adjusted the calibration of the method, and Medic24 applied for a third evaluation of the *i*-CHROMA system in both hospital and primary health care centres.

The major changes in the *i*-CHROMA instrument from 2008 to 2010 are:

	SKUP/2008/61	SKUP/2011/90
Calibration functions	One	Two
Calibration function points	Two	Seven
Serum/plasma detection	No	Yes
Sample volume, serum / whole blood	10 µL/15 µL	10 µL/10 µL
Operation steps		One step less
Control samples	No	Yes

Helena Olkkonen-Ure, Medic24, applied to SKUP in 2010 for a repeated evaluation of the *i*-CHROMA reader with CRP test strips. SKUP accepted to carry out this evaluation on behalf of Medic24.

3.5.2. *Meetings, contract, and protocol*

A meeting with Mr. Joung Dae Moon from Boditech, Korea and Helena Olkkonen-Ure, Medic24, Norway, was held at Hillerød Hospital on the 19th of March 2010.
In the meeting, the protocol was discussed and approved.
Stine Beenfeldt Weber was taught to operate the *i*-CHROMA instrument. Capillary samples, venous whole blood EDTA samples, and control samples were analysed on the instrument.
The contract was signed the 19th of March 2010.

3.5.3. *Time schedule*

The evaluation period:

Hospital laboratory	26th of April to the 29th of September 2010
Primary health care centre 1	4th of May to the 13th of September 2010
Primary health care centre 2	3rd of May to the 15th of July 2010

3.5.4. *Collection of samples*

57 outpatients and 87 hospital admitted patients who were to have their P—CRP measured routinely, agreed to participate in the hospital evaluation. At first, all 144 individuals had one capillary test performed on the *i*-CHROMA. Based on this result, 114 of them continued to have a second capillary test performed. 30 patients were excluded due to an excessive amount of patients with P—CRP results measured as <2,5 mg/L, which is the minimum value measured by *i*-CHROMA. Two skin punctures were made to collect the two samples. The second blood drop was used for analysing on the *i*-CHROMA.

Following this, venous samples (one tube of Z Serum Separator gel and Clot Activator and one K_3EDTA tube in one skin perforation) were drawn. The tubes were inverted 8-10 times to ensure thorough mixing.
Four lot numbers were by mistake sent from Chorea instead of three, they were all used in the evaluation.

3.5.5. *Evaluation sites and persons involved*

The hospital evaluation took place in Hillerød Hospital, Dept. of Clinical Biochemistry.
Stine Beenfeldt Weber, SKUP/Hillerød, did the practical work including collecting capillary and venous samples for the evaluation.

The primary health care evaluation took place in centres that normally use capillary samples to analyse P—CRP. Laboratory consultant Inge Lykke Pedersen was contact person to the primary health care centres regarding their routine P—CRP analysis.

Primary health care centre 1: Gribskov Lægecenter, Lundehuset, Tisvildevej 28, 3210 Vejby. This primary health care centre consists of five general practitioners, two nurses, two secretaries, and one biomedical laboratory scientist. At this centre, the laboratory technician does all the laboratory work, and therefore alone handled the samples for the evaluation.
Primary health care centre 2: Lægerne i Græsted, Skovsmindeparken 1, 3230 Græsted. At the primary health care centre, there is one general practitioner, one secretary, and two nurses. The nurses both do laboratory work, but only one handled the samples for the evaluation.

Esther Jensen made the statistical calculations.

Table 4. Evaluation sites and persons involved

Place	Person	Title	Task
Hillerød Hospital	Esther A Jensen	Physician	Author of the report
Hillerød Hospital	Steen Ingemann Hansen	Civil engineer	Responsible for comparison method
Hillerød Hospital	Grethe Schrøder	Biomedical laboratory scientist	Responsible for comparison method
Hillerød Hospital	Stine Beenfeldt Weber	Cand. Scient.	Hospital testing and contact person for primary health care. Co-author of the report
Hillerød Hospital	Inge Lykke Pedersen	Biomedical laboratory scientist	Consultant for primary health care quality
Primary Health Care	Helle Gonzales	Biomedical laboratory scientist	Primary health care testing
Primary Health Care	Lene Heller	Nurse	Primary health care testing

3.5.6. *Blood sampling devices*

The capillary punctures were performed with the lancet Owen Mumford, Unistik®3 Extra, Gauge 21G (0,81mm), depth 2,0 mm.
Venous blood for P—CRP measurements with the comparison method was drawn into 4 mL Vacuette Greiner bio-one from Greiner containing Z Serum Separator gel and Clot Activator.
Venous blood for measuring P—CRP on the *i*-CHROMA and for measuring P-hematocrit on Sysmex XE-5000 was drawn in 3 mL Vacuette Greiner bio-one from Greiner containing K_3EDTA.

3.6. The evaluation procedure

3.6.1. *The evaluation model*

The evaluation in the hospital laboratory and two primary health care centres deals with:

- Documentation of trueness of the comparison method
- Determination of imprecision of the *i*-CHROMA CRP system with capillary whole blood samples and venous whole blood samples from more than 100 individuals measured in duplicates with the *i*-CHROMA CRP system
- Determination of the deviation of the *i*-CHROMA CRP system from the comparison method with capillary whole blood samples and venous whole blood samples from more than 100 individuals measured in duplicates with the *i*-CHROMA CRP system
- To ensure that the instrument measures equally correct in both the low and high P—CRP concentrations. Therefore a concentration distribution with 50-60% of the measurements above 15 mg/L is ensured
- Determination of the imprecision and accuracy with 40 patient samples in each of two primary health care centres
- Evaluation of user-friendliness of *i*-CHROMA in hospital laboratory and primary health care centres
- Evaluate the use of the Medic24 control material
- Investigation of the influence of hematocrit for measurement performed on i-Chroma with samples from hospitalised patients.

It was not part of the original protocol to adjust for the hematocrit and recalculate the P—CRPs because the doctors at the primary health care centres do not normally have access to hematocrit concentrations.
The samples from the hospitalised patients possibly have a lower hematocrit than the typical CRP-sample in the primary health care centre. The number of hospitalised patients could therefore have an impact on the evaluation results, since the *i*-CHROMA is sensitive to hematocrit in the samples. To make sure, that an error was not introduced by including hospitalised patients, the influence of hematocrit was investigated.

The hospital laboratory evaluation was performed in Hillerød Hospital. The capillary samples and the venous EDTA sample from each patient were measured in duplicates using the same *i*-CHROMA instrument and test strips with the same lot number. Serum samples from the same patients were measured with the comparison method. A total of six CRP-measurements were made on each patient in the evaluation.

3.6.2. *Evaluations procedure in the hospital laboratory (standardised and optimal conditions)*

Training

Stine Beenfeldt Weber was trained by Boditech Med Inc, Korea on the 19th of March 2010. Capillary samples, venous EDTA samples and control samples were analysed using the *i*-CHROMA CRP system in the Department of Clinical Biochemistry, Hillerød Hospital. Everyone agreed that Stine performed the analysis correctly.

Recruitment of patients
To insure a sufficient number of high P—CRP values, patients admitted to Department of Pulmonary and Infectious Diseases at Hillerød Hospital were included in the evaluation as well as outpatients.
57 outpatients and 87 hospital admitted patients who were to have their P—CRP measured according to the normal routine agreed to participate in the hospital evaluation.

Handling of samples and measurements
At first, all individuals had one capillary test performed on the *i*-CHROMA. Based on this result, most individuals continued to have a second capillary test performed. Some were excluded because the P—CRP results measured were low, <2,5 mg/L, which is the minimum value measured by *i*-CHROMA. Two skin punctures were made to collect the two samples. The second blood drop was used for analysing on the *i*-CHROMA. Following, venous samples (one tube of Z Serum Separator gel with Clot Activator and one EDTA tube in one skin perforation) were drawn. The tubes were inverted 8-10 times to ensure thorough mixing
Four lot numbers of P—CRP test strips and buffers were used in the evaluation.

Analysing with the i-CHROMA
The samples were analysed in duplicates with the *i*-CHROMA CRP system, first the two capillary whole blood samples, then the two venous EDTA whole blood samples, a total of four measurements on the *i*-CHROMA instrument for each patient. The EDTA samples were measured on the *i*-CHROMA on the same day as the capillary samples.
The instruction manual was followed, see attachment 2. For capillary samples, the second blood drop was used.

Analysing with the comparison method
After routine analysing with the comparison method, the samples were reanalysed on the other comparison method instrument used in the evaluation. The time from blood sampling to analysis was maximum 8 hours.

Number of samples:
Samples were collected until the following criteria regarding P—CRP measured values, using the comparison method, were obtained:

Table 5. The comparison method, distribution of the concentrations in the samples

	% of total, concentration				
P—CRP (mg/L)	<5	<15	> 15	>50	>100
number at least	5	5-10	≥60	≥15	≥5

The samples in the evaluation were to be collected on more than 20 individual days.

Comparison method, external QC
Certified Reference Material (CRM) 470 was used on two separate days after the testing.
The External QC from Labquality and DEKS was also used, data is shown later.

Quality assurance with the i-CHROMA CRP system
A control material from Boditech Med Inc. was analysed every day.

Analysing the hematocrit
Prior to the analysing on the *i*-CHROMA CRP system, the EDTA tube was analysed on the Sysmex XE-5000 in the department to get a hematocrit value.

Handling the measurements
Stine Beenfeldt Weber registered all the results in Excel. If an instrument showed an error message, a new measurement was made on the same instrument.

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

3.6.3. *Evaluation procedure in the primary health care*

Training
The supplier was responsible for training on the *i*-CHROMA. Medic24 gave training to the staff in the two primary health care centres. When the evaluation began, the evaluators had to handle *i*-CHROMA on their own without any supervision or correction from the manufacturer/supplier. If there were any questions, these were addressed to SKUP. Helena Olkkonen-Ure from Medic24 gave training at both centres on the 29th of April 2010.

Recruitment of patients
80 patients, that were going to have a routine P—CRP measurement, agreed to participate and have two capillary P—CRP measurement performed. Participation was voluntarily and verbal consent was considered sufficient. Capillary samples were collected from 40 patients in each primary health care centre.

Handling of samples and measurements
The 80 patients had two capillary samples taken in two skin penetrations. The second blood drop was used for analysing on the *i*-CHROMA. The capillary samples were measured on the *i*-CHROMA immediately.
The samples from the 40 patients in each primary health care centre were measured on one instrument and using two different lot numbers, in a way so that samples from one patient were measured with test strips from the same lot number. Two lot numbers were used in each of the primary health care centres in the evaluation.
One venous sample (a tube of Z Serum Separator gel and Clot Activator) per patient was collected for measurements on the comparison method. This sample was sent with the routine transportation system for blood samples to the Department of Clinical Biochemistry, Hillerød Hospital. The sample was sent in a separate envelope.
All results were registered and signed for by the evaluator. If an instrument showed an error code while analysing a sample, a new measurement was made if possible. The error codes were recorded. Data was recorded in a form produced by Stine Beenfeldt Weber.

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

4. Statistical expressions and calculations

The definitions in this section are taken from the International Vocabulary of Metrology (VIM) [15].

4.1. Statistical terms and expressions

4.1.1. *Precision*

Definition: Precision is the closeness of agreement between measured quantity values obtained by replicate measurements on the same or similar objects under stated specified conditions.

Precision is descriptive in general terms (good, acceptable, poor e.g.) and measured as imprecision. Imprecision is expressed by means of the standard deviation (SD) or coefficient of variation (CV). SD is reported in the same unit as the analytical result and CV is usually reported in percent.

Repeatability is the agreement between the results of consecutive measurements of the same component carried out under identical measuring conditions (within the measuring series). Reproducibility is the agreement between the results of discontinuous measurements of the same component carried out under changing measuring conditions over time. The reproducibility includes the repeatability.

To be able to interpret an assessment of precision, the precision conditions must be defined. The "specified conditions" can be, for example, repeatability, intermediate precision, or reproducibility conditions of measurement. The precision conditions in this evaluation are close to the defined *repeatability* and *reproducibility* conditions, and the imprecision is expressed as repeatability CV and reproducibility CV. The imprecision is summarised in tables.

4.1.2. *Accuracy*

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

Inaccuracy is a measure of the deviation of a single measurement from the true value, and implies a combination of random and systematic error (analytical imprecision and bias). Inaccuracy, as defined by a single measurement, is not sufficient to distinguish between random and systematic errors in the measuring system. Inaccuracy can be expressed as allowable deviation. The inaccuracy is illustrated by difference-plots with quality goals for the allowable deviation shown as deviation limits in percent.

4.1.3. *Trueness*

Definition: Trueness is the closeness of agreement between the average of an infinite number of replicate measured quantity values and a reference quantity value.

Trueness is measured as bias (systematic errors). Trueness is descriptive in general terms (good, poor), whereas bias is the estimate, reported in the same unit as the analytical result or in percent. The bias at different concentration levels is summarised in tables.

4.2. Statistical calculations

4.2.1. *Statistical outliers*

All the results are checked for outliers according to Burnett [16], with repeated truncations. The model takes into consideration the number of observations together with the statistical significance level for the test. The significance level is often set to 5%, as it is in this evaluation. Where the results are classified according to different concentration levels, the outlier testing is done at each level separately. Statistical outliers are excluded from the calculations. Possible outliers will be commented on under each table.

4.2.2. *Calculations of imprecision based on duplicate results*

The imprecision was calculated with the following formula:

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

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

This formula is preferred when estimating CV over a large concentration interval within which the CV is assumed reasonable constant.

The assumption for using this formula is that there is no systematic difference between the 1st and the 2nd measurement.

4.2.3. *Calculation of trueness*

To measure the trueness of the results at *i*-CHROMA, the average bias at three concentration levels is calculated based on the results obtained under standardised and optimal measuring conditions. A paired t-test is used with the mean values of the duplicate results at the comparison method and the mean values at *i*-CHROMA.

4.2.4. *Calculation of accuracy*

To evaluate the accuracy of the results at *i*-CHROMA, the agreement between *i*-CHROMA and the comparison method is illustrated in difference plots. In the plots, the x-axis represents the mean value of the duplicate results at the comparison method. The y-axis shows the difference between the first measurement at *i*-CHROMA with four lots and the mean value of the duplicate results at the comparison method.

5. Results and discussion

It is a decision in SKUP that the number of patients in a SKUP evaluation under optimal conditions in a hospital evaluation should never be less than 100. The reason for this is that the evaluation should have high statistical impact. Furthermore the challenge in this evaluation is to get an approriate amount of results above the reference interval. Results in the reference interval are given as <2,5 mg/L in the *i*-CHROMA method.

5.1. Number of samples

114 (58 women and 56 men) individuals that were going to have a P—CRP measured participated with capillary duplicate measurements on the *i*-CHROMA instrument.
An additional 30 patients accepted to participate. However, their fist CRP-measurement on *i*-CHROMA was low and the patients were not included in the evaluation. The low value excluded them from further investigation, since it was important to get the right distribution of measurements.
There should be 114 duplicate measurements on the comparison method. However, only 112 were duplicates and two were singletons. The singletons are used for calculating allowable deviation. The duplicates always originate from two comparison method instruments. One instrument broke down during the evaluation and was replaced with another. The first two results in the new instrument were outliers (P—CRP 55,9 and 65,0 mg/L) and (P—CRP 87,9 and 112,0 mg/L). These duplicate results are not used in the evaluation.
Of the 114 capillary duplicate measurements in *i*-CHROMA there were three outliers (46,3 and 38,9 mg/L), (131,8 and 81,9 mg/L) and (235,1 and 285 mg/L). These duplicate results are not used for bias calculations in the evaluation.
Of the 114 individuals, five were, by mistake, not measured using venous EDTA blood on the *i*-CHROMA.

The distribution of the lots was: 20 patients were measured using lot 3, 29 patients were measured using lot 4, 37 patients were measured using lot 5, and 28 patients were measured using lot 10.
The P—CRP concentrations obtained with the comparison method are shown in table 6. The number of samples are shown in table 7.

Table 6. The comparison method, distribution of the concentrations in the 144 samples

P—CRP (mg/L)	<5	5 - 15	15 - 50	50 - 100	>100	in total
n accepted	45	24	29	23	23	144
n included*	22	17	29	23	23	114

* a total of two samples were only measured once on the comparison method

Table 7. Number of test used on the *i*-CHROMA instrument in the evaluation

The evaluation in a hospital laboratory	Number of test strips used
Measurements on capillary whole blood samples	114 x 2 + 30 = 258
Measurements on venous whole blood samples	109 x 2 = 218
Measurements on control samples	79
Invalid tests	
n total	***~555***

5.1.1. *Failed measurements*

No error codes occurred during the evaluation when measuring control samples, capillary samples, or venous samples. The percent of invalid tests was therefore 0%.

5.1.2. *Missing or excluded results*

The first samples were only measured as capillary samples and not as venous EDTA samples in the *i*-CHROMA CRP system. The number of missing and excluded results is explained under the tables and figures.

5.2. Analytical quality of the selected comparison method

5.2.1. *The precision of the comparison method*

Table 8. Repeatability of the comparison method with serum patient samples

Level	Comparison method interval P—CRP, mg/L	n	Outliers	Comparison method mean P—CRP, mg/L	CV % (95 % C.I.)
Low	0,0 — 0,9	11	0	—	—
	1,0 — 2,4	6	0	1,4	13,9 (9,0 — 30,7)
	2,5 — 13,4	21	0	7,3	3,3 (2,6 — 4,8)
Medium	13,5 — 56,4	38*	1	29,7	2,4 (2,0 — 3,1)
High	56,5 — 264,6	38*	1	130,1	2,1 (1,7 — 2,8)
All	1,0 — 264,6	103	2	54,8	4,2 (3,7 — 4,9)

* Two measurements were not performed in duplicate. According to Burnett, there were two outliers: (P—CRP 55,9 and 65,0 mg/L) and (P—CRP 87,9 and 112,0 mg/L). The given numbers of results (n) are counted before the exclusion of outliers. Mean and CV are calculated after the exclusion of outliers.

Discussion: The calculated CV values are measures of imprecision under intermediate conditions, as they also include some additional variance arising from the fact, that all the duplicate measurements originates from two different instruments and some of them were measured on two different days.
In table 8, the two outliers on the comparison method originate from the first day – the first hour - the Integra 1b was used.

The “low” comparison method results in table 8 are divided into three groups. The laboratory normally reports very low results to clients as “<1,0 mg/L”. The lowest concentration *i*-CHROMA can measure is 2,5 mg/L. The comparison method results between 1,0 mg/L and 2,5 mg/L were all <2,5 mg/L on *i*-CHROMA. Therefore, all comparisons between the comparison method and the *i*-CHROMA are made when measurements on the *i*-CHROMA and on the comparison method produced results above 2,5 mg/L.

5.2.2. *The trueness of the comparison method*

Table 9. The bias of the comparison method

Certified Reference Material (CRM) 470						
Date	**Comparison instrument**	**n**	**measured mg/L**	**assigned mg/L**	**CV %**	**Bias %**
07-10-2010	Integra I	5	42,2	39,2	1,5	7,7
08-10-2010	Integra II	4	41,6	39,2	0,7	6,1
		9	41,9	39,2	1,4	7,0

The results of the comparison method in this report are adjusted for a bias with the coefficient (k) 0,934. The coefficient (k) is based on the results with the Certified Reference Material (CRM) 470 material (table 9). To reach the assigned concentration 39,2 mg/L for the measured concentration 41,9 mg/L, k = 0,934.

Table 10. The comparison method, compared with the Labquality EQA program for P—CRP

	Comparison method	**Turbidimetric methods**			**All methods**		
Survey 2010	**P—CRP mg/L**	**Mean, P—CRP mg/L**	**n**	**Deviation%**	**Mean, P—CRP mg/L**	**n**	**Deviation%**
February	76	73	151	4,1	75	181	1,3
March	76	73	225	4,1	75	301	1,3
April	27	25	167	8,0	26	202	3,8
May	147	136	216	8,1	138	287	6,5
June	19	18	161	5,6	19	192	0,0
August	42	37	180	13,5	38	220	10,5
September	26	25	220	4,0	26	301	0,0
Mean				**6,8**			**3,4**

Discussion: Table 10 shows that the deviation of the comparison method compared to the turbidimetric methods 6,8% and compared to all methods the deviation of the comparison method is 3,4%.
The Cobas Integras are part of the turbidimetric group and not in a subdivided group. Labquality concentrations are in the range 19 mg/L to 147 mg/L and the deviation is constant throughout the range. The Department of Clinical Biochemistry in Hillerød has accepted a bias up to 10% and has had a small positive bias on all seven Integra instruments in all three hospital departments sorting under the Department of Clinical Biochemistry in Hillerød (Hillerød, Frederikssund, and Helsingør) since 2002.

The CV% for the concentration of 39,2 mg/L with the comparison method was 1,4% which is less than the ”allowed 5%”.

5.2.3. *Internal quality control with the comparison method*

The internal control samples were run daily on all comparison method instruments using DEKS controls. Below the results are shown for one of the comparison method instruments. The results for the other instruments were similar (not shown). The imprecision in a duplicate result on the comparison method always originate from two different instruments.

Table 11. Internal quality control result of P—CRP on one of the comparison method instruments in 2010

	Control HK02			**Control HK10**			**Control HK06**		
month 2010	**mean, mg/L**	**n**	**CV%**	**mean, mg/L**	**n**	**CV%**	**mean, mg/L**	**n**	**CV%**
January	84,8	20	3,0				26,8	30	2,8
February	82,2	19	2,8				27,8	24	1,1
March	80,9	18	1,5				26,7	28	2,8
April	82,0	14	2,8				27,0	16	1,8
May	84,9	10	2,9				27,6	21	1,9
June	85,0	17	2,9	25,0	24	4,4			
July	88,0	19	1,7	25,0	27	1,5			
August	86,0	22	1,7	25,0	28	1,8			
September	86,0	22	1,7	25,0	27	1,3			
October	86,5	17	2,4	25,0	24	2,4			
November	85,8	19	1,2	25,5	30	3,2			
December	86,9	20	1,5	25,5	27	1,9			
Mean	84,9	18,1	2,2	25,1	26,7	2,4	26,6	26,7	2,4

The CV% for the concentration of 84,9 mg/L with the Integra was 2,2% during the 12 months while the concentration 25,1 and 26,6 mg/L had a CV% of 2,4%, all less than the ‘allowed 5%’.

5.3. Analytical quality of *i*-CHROMA used in a hospital laboratory

5.3.1. *Internal quality control*

During the evaluation, a control material for one level was used on *i*-CHROMA. The material was from Medic24 and manufactured to be used on all kinds of CRP instruments. The control had a mean of 40 mg/L with a range of 30 – 50 mg/L, but no certified target value.
The reproducibility was assessed with the control material and four lot numbers on 33 individual days. Control material may have other matrix effects than whole blood, and may therefore give other results than results achieved with blood. The measurements were carried out daily during the evaluation period. The reproducibility of *i*-CHROMA is shown in table 12.

Table 12. Internal quality assurance of *i*-CHROMA during the evaluation

Date	Medic24 CRP Control material, mg/L	Date	Medic24 CRP Control material, mg/L
26-04-2010	34,9	09-07-2010	34,0
05-05-2010	35,5	12-07-2010	32,5
10-05-2010	35,5	13-07-2010	32,0
12-05-2010	33,2	14-07-2010	34,4
25-05-2010	33,1	15-07-2010	33,3
26-05-2010	33,0	09-08-2010	34,4
27-05-2010	34,8	10-08-2010	33,8
31-05-2010	33,7	12-08-2010	34,0
01-06-2010	34,5	18-08-2010	33,4
03-06-2010	34,2	19-08-2010	35,5
04-06-2010	32,2	08-09-2010	33,9
08-06-2010	33,9	09-09-2010	35,1
24-06-2010	31,9	13-09-2010	34,8
05-07-2010	34,1	14-09-2010	34,8
06-07-2010	32,9	28-09-2010	32,6
06-07-2010	33,3	29-09-2010	31,8
08-07-2010	34,1		

The control material from Medic24 was analysed daily, n= 33, P—CRP mean 33,8 mg/L. CV%=3,1. The CV% is lower than the goal for genuine samples of <10,0%.

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

Two capillary samples were taken from 114 individuals for measurements on *i*-CHROMA. The results are checked to meet the assumption that there is no difference between the first and the second measurement. Table 13 shows that no systematic difference was pointed out between the paired measurements.

Table 13. Comparison of the 1st and 2nd P—CRP measurement on *i*-CHROMA

Sample material	n	Mean 1st measurement (P—CRP, mg/L)	Mean 2nd measurement (P—CRP, mg/L)	Mean difference 1st - 2nd measurement (P—CRP, mg/L)	95% CI for the mean difference, (P—CRP, mg/L)
capillary	93	60,2	59,3	0,87	-0,2 - +1,9
venous EDTA	89	62,8	62,0	0,75	-0,3- +1,8

5.3.3. *The precision of i*-CHROMA

Table 14. Repeatability of *i*-CHROMA with capillary samples in the hospital laboratory

Level	**Comparison method P—CRP interval (mg/L)**	**n**	**Excluded results**	***i*-CHROMA P—CRP mean (mg/L)**	***i*-CHROMA CV% (95% CI)**
Low	0,0 — 13,5	38*	0	8,0	4,5 (3,5 — 6,6)
Medium	13,5 — 56,4	38	1**	30,0	3,7 (3,0 — 4,8)
High	56,5 — 264,6	38	2***	134,9	4,9 (4,0 — 6,4)
All	1,0 — 264,6	114*	3	59,1	4,3 (3,8 — 5,1)

*18 samples were measured as <2,5 mg/L on *i*-CHROMA. ** one outlier (46,3 and 38,9 mg/L) *** two outliers (131,8 and 81,9 mg/L) and (235,1 and 285 mg/L) with *i*-CHROMA. Mean and CV are calculated after the exclusion of the two outliers and the 18 samples.

Table 15. Repeatability of *i*-CHROMA with venous samples (whole blood EDTA) in the hospital laboratory

Level	**Comparison method P—CRP interval (mg/L)**	**n**	**Excluded results**	***i*-CHROMA P—CRP mean (mg/L)**	***i*-CHROMA CV% (95% CI)**
Low	0,0 — 13,5	38*	0	7,8	4,8 (3,7 — 4,8)
Medium	13,5 — 56,4	38**	1**	29,7	2,9 (2,4 — 3,9)
High	56,5 — 264,6	38***	0	125,3	4,3 (3,6 — 5,7)
All	1,0 — 264,6	114*	0	62,4	3,9 (3,5 — 4,7)

*19 samples were measured as <2,5 mg/L with the *i*-CHROMA. ** one outlier (49,0 and 43,3 mg/L) and two venous samples were not measured *** three venous samples were not measured. Mean and CV are calculated with 19, 35 and 35 samples in the groups low, medium, and high.

Discussion: The calculated CV values are measures of repeatability, but they also include some additional variance arising from the fact that the duplicate measurements originates from four lot numbers of various age.

The lowest concentration *i*-CHROMA can measure is 2,5 mg/L. There is no difference in CV% in repeatability for various concentration levels.
SKUP quality goal (CV% less than 10%) was fulfilled for all concentration levels with four lots no matter if it was a new lot or a lot about to expire.

5.3.4. *The trueness of i*-CHROMA

Table 16. Bias of *i*-CHROMA CRP with capillary patient samples in hospital

Level group	Comparison method P—CRP interval (mg/L)	n	Ex-cluded results	Comparison method P—CRP mean (mg/L)	Bias mg/L (95% CI)	Bias % (95% CI)
Low	0,0 — 13,5	38*	0	8,0	+0,4 +0,1 — +0,7)	+6,6 (+2,8 — +10,4)
Medium	13,5 — 56,4	38	1+1**	32,4	0,0 (−1,5 — (−1,6))	+3,3 (+1,0 — +7,6)
High	56,5 — 264,6	38	2+1***	120,3	−6,6 (−13,0 — (−0,2))	−6,2(−10,2 — +2,2)
All	1,0 — 264,6	114*	5	66,3	−2,4 (−5,0 — +0,1)	+0,4 (−2,2 — +2,9)

*18 samples were measured as <2,5 mg/L with the *i*-CHROMA. ** one outlier (46,3 and 38,9 mg/L) with i-CHROMA and one on the comparison method *** two outliers (131,8 and 81,9 mg/L) and (235,1 and 285 mg/L) with the *i*-CHROMA and one with the comparison method. Mean and bias are calculated after the exclusion of the outliers and the 18 samples.

Table 17. Bias of *i*-CHROMA CRP with venous patient samples in hospital

Level group	Comparison method P—CRP interval (mg/L)	n	Ex-cluded results	Comparison method P—CRP mean (mg/L)	Bias mg/L (95% CI)	Bias % (95% CI)
Low	0,0 — 13,5	38*	0	7,8	0,0 (−0,3 — +0,3)	+1,3 (−2,8 — +5,5)
Medium	13,5 — 56,4	38	1+1**	29,2	−1,1 (−2,8 — +0,5)	−1,0 (−5,3 — +3,3)
High	56,5 — 264,6	38	1***	125,3	−8,8 (−15,1 — (-2,4))	−7,6 (−11,4 — +3,7)
All	1,0 — 264,6	114*	3	62,2	-3,8 (−6,4 — +1,1))	−3,0 (−5,5 — (-0,4)

*19 samples on *i*-CHROMA had at least one result <2,5 mg/L. ** one duplicate was excluded on *i*-CHROMA, one on the comparison method, and two samples were not measured on *i*-CHROMA. *** one duplicate sample was excluded on the comparison method, three samples were not measured as venous samples. Mean and bias are calculated after the exclusion of the outliers, the missing results, and the 18 samples with results lower than 2,5 mg/L.

Discussion: The Danish quality goal (Bias less than 10%) was fulfilled for all concentrations for capillary and venous samples. SKUP has no separate goals for bias, even though bias is part of allowable deviation.
It seems as if there is a matrix effect in the low concentrations between capillary and venous samples. The capillary samples are 0,4 mg/L higher than the venous samples (+6,6% and 1,3%). However, the difference is not significant.

5.3.5. *The accuracy of i*-CHROMA

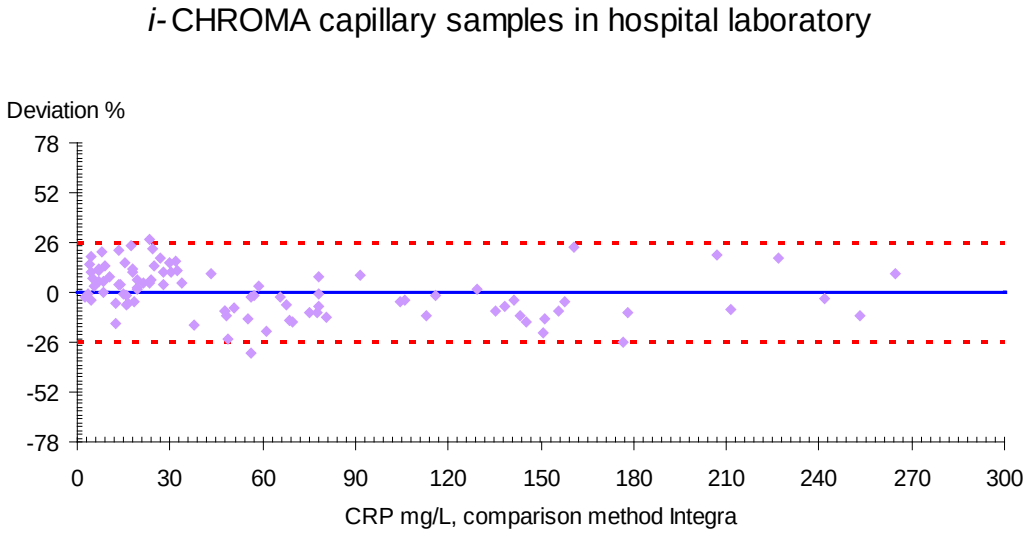

Figure 4. Difference plot showing the accuracy of the *i*-CHROMA P—CRP results measured in capillary whole blood samples in the hospital laboratory. The x-axis represents the mean value of the duplicate results with the comparison method. The y-axis shows the deviation in percent between the first measurements on the *i*-CHROMA and the mean value of the duplicate results with the comparison method, n = 114 (18 of the samples each showed the result <2,5 mg/L on the *i*-CHROMA instrument). Stippled lines represent allowable deviation ±26%.

Comments: 95% of the results should be within the allowable deviation to fulfil the quality goals for allowable deviation <±26%.
Capillary samples: Only two of 114 results exceed the maximal allowed deviation of ±26%.
Conclusion: In the hospital laboratory, the capillary sample results fulfil the quality goals for allowable deviation.

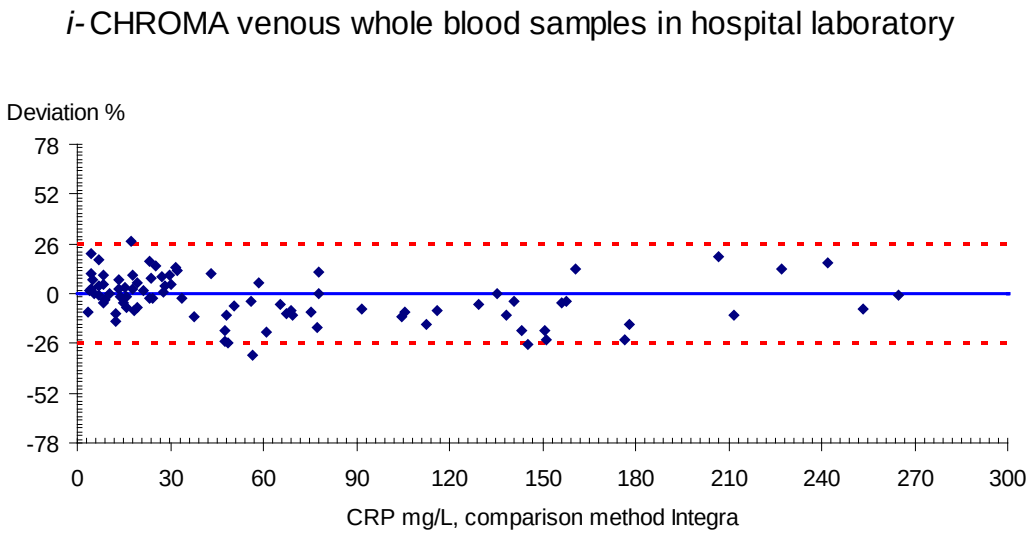

Figure 5. Difference plot showing the accuracy of the *i*-CHROMA P—CRP results measured in venous whole blood samples in the hospital laboratory. The x-axis represents the mean value of the duplicate results with the comparison method. The y-axis shows the deviation in percent between the first measurements on the *i*-CHROMA and the mean value of the duplicate results with the comparison method, n = 114 (19 of the samples each showed the result <2,5 mg/L on the *i*-CHROMA instrument). Stippled lines represent the allowable deviation ±26%.

Comments: 95% of the results should be within the allowable deviation to fulfil the quality goals for allowable deviation of <±26%.
Venous samples: 3 of 109 results exceed the maximal allowed allowable deviation (±26%). Thus, the venous sample results in hospital laboratory fulfil the quality goals for allowable deviation of less than ±26%.

Discussion: Discussion: When figure 5 and 6 is compared, it seems that there is a positive deviation in the capillary concentrations below 35 mg/L. This deviation is, however, not significant (Tables 16,17).

5.3.6. *The accuracy of i-CHROMA with different lots of test strips*

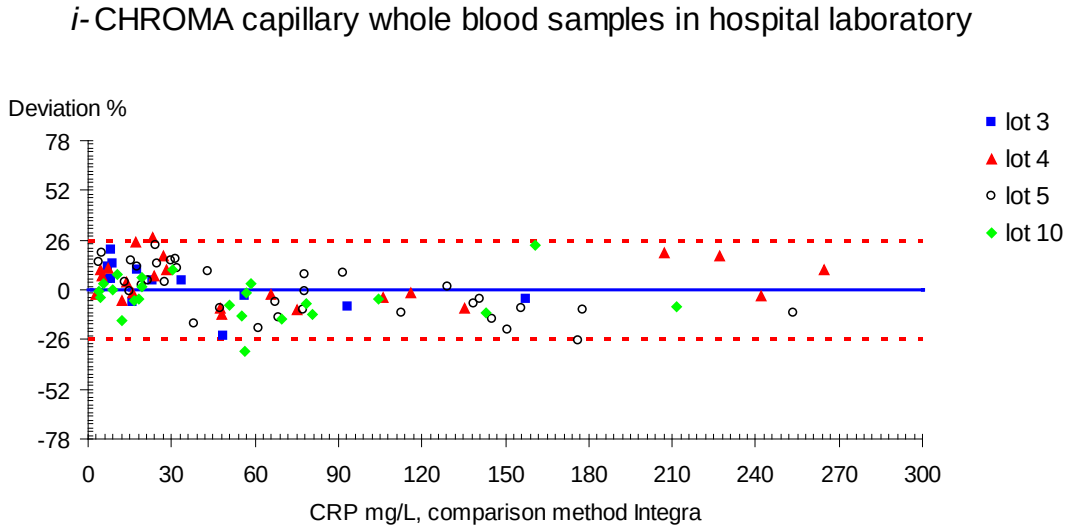

Figure 6. Difference plot showing the accuracy of the *i*-CHROMA P—CRP results measured in capillary whole blood samples in the hospital laboratory. The x-axis represents the mean value of the duplicate results with the comparison method. The y-axis shows the deviation in percent between the first measurements on the *i*-CHROMA and the mean value of the duplicate results with the comparison method, n = 114 (18 of the samples each showed the result <2,5 mg/L on the *i*-CHROMA instrument). Stippled lines represent the allowable deviation ±26%. Results are shown with different symbols depending on used lot of test strip.

Results from the venous samples showed the same (data not shown)

Comments: There is no extreme deviation in the evaluation. The four lots of tests used in the hospital evaluation are shown in figure 6. It is demonstrated, that none of the lots deviate compared to the other lots.

5.3.7. *Interference from hematocrit*

Most patients with severe infections have a low hematocrit compared to healthy individuals or outpatients. A possible interference from hematocrit was checked by plotting the hematocrit-values on the X-axis and the deviations from the comparison method on the Y-axis in a diagram.

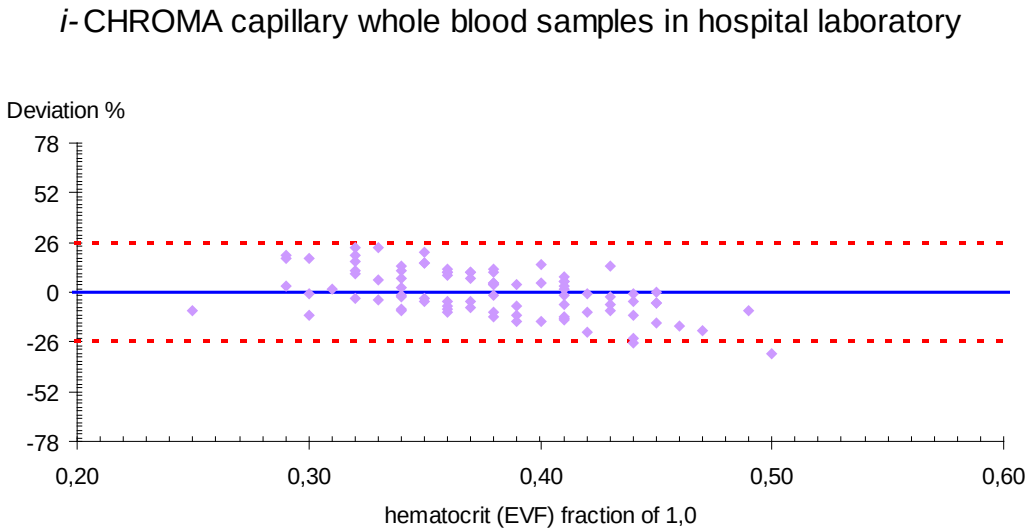

Figure 7. Plot from the hospital evaluation showing the deviation of the *i*-CHROMA P—CRP results in capillary whole blood as a function of the patients hematocrit. The x-axis represents the hematocrit value of the sample. The y-axis shows the deviation in percent between the first measurements on the *i*-CHROMA and the mean value of the duplicate results with the comparison method, n = 114 (18 of the samples showed the result <2,5 mg/L on the *i*-CHROMA instrument). Stippled lines: allowable deviation ±26%.

Discussion: The primary health care centres do not have access to hematocrit concentrations during the consultations, therefore it was not part of the evaluation to recalculate the P—CRP's after adjusting for hematocrit.

The plot shows the expected effect on the P—CRP results when the instrument uses a fixed hematocrit value of 0,40. In this evaluation it is seen that a fixed hematocrit is acceptable because the extreme hematocrit values do not give results that deviate more than 26%.

Results from venous samples show the same (data not shown).

5.4. Analytical quality of *i*-CHROMA in primary health care

5.4.1. *Internal quality control*

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

Table 18. Reproducibility of *i*-CHROMA with control material at the primary health care centres

Primary health care centre	n	mean P—CRP mg/L	CV%
primary care health centre 1	21	38,5	24,1
primary care health centre 2	25	31,5	16,1

Discussion: The reproducibility CV with the recommended control material was 16,1 and 24,1% in primary health care – much higher than in the hospital laboratory where the CV% with the same control material in the same time period was 3,1%. Both primary health care centres were contacted during the evaluation period to investigate if the CV in the measurement results of the control samples was possible to improve. One centre had a visit from Stine Beenfeldt Weber to assess possible pitfalls. It was pointed out that it is important to hold the buffer cup at a distance from the test strip when squeezing out the two drops for sampling. Otherwise, accidental suction and re-uptake of some of the sample material into the buffer cup might occur. Other pitfalls are pointed out in 5.5.2. However, there was no difference in the quality of control measurement results before and after the contact. Both centres explained it was very difficult to know when the sample volume was correct. It is a question, if colourless control material is suitable for primary health care.

5.4.2. *The precision of i*-CHROMA *in primary health care centres*

The duplicate measurements on *i*-CHROMA in primary health care were done on capillary samples. The results are seen below for the two centres. The sampling was performed within 4,5 months in primary health care centre 1 and within 2,5 months in primary health care centre 2.

Table 19. Repeatability of *i*-CHROMA on capillary samples in the primary health care centre 1

Level	Comparison method interval P—CRP, mg/L	n	Excluded results	*i*-CHROMA mean P—CRP, mg/L	CV% (95% CI)
Primary health care centre 1					
Low	<1,0	4*	0	<2,5	—
	1,0 — 5,5	16*	0	3,8	4,6 (2,9 — 11,3)
High	5,9 — 130	20	2	21,5	5,9 (4,5 — 8,7)
All	1,0 — 130	40	2	17,8	5,7 (4,5 — 7,9)

**i*-CHROMA showed the result <2,5mg/L for each of 15 samples. The two excluded results were outliers: One sample on the comparison method (19,2 and 23,0 mg/L and one on *i*-CHROMA (189 and 214 mg/L).

Comments: The 15 samples that showed <2,5 mg/L in *i*-CHROMA corresponded well with the comparison method, where 14 of them were <2,5 mg/L. The CV% in primary health care centre 1 fulfil the quality goals with a CV <10%. There is a discrepancy between the CV of the genuine patient samples (5,7%) and the CV of the 21 control samples (24,1%). The CV for the genuine samples is not different from the CV in the hospital evaluation, which is 4,3% (table 14).

Table 20. Repeatability of *i*-CHROMA on capillary samples in the primary health care centre 2

Level	**Comparison method interval P—CRP, mg/L**	**n**	**Excluded results**	***i*-CHROMA mean P—CRP, mg/L**	**CV% (95% CI)**
Primary health care centre 2					
Low	<1,0	8	0	<2,5	—
	1,0 — 2,2	12	0	<2,5	—
'High'*	2,4 — 4,1	7	0	<2,5	—
High	3,9 — 177	14	4**	20,4	15,0 (10,5 — 26,5)

*Seven of the 21 highest concentrations had a concentration below 2,5mg/L on *i*-Chroma. **One of the excluded results were <2,5 mg/L in both duplicates while the comparison method results were 11,5 mg/L twice. Three samples showed one result <2,5 mg/L and the other result 3,4 mg/L, 5,4 mg/L, and 17,4 mg/L, respectively.

The calculated CV values are practically measures of repeatability, but they also include some additional variance arising from the use of two lot numbers. The results in the comparison method were analysed using two instruments.

Discussion: The imprecision in primary health care centre 2 was very high compared to the hospital and the primary health care centre 1. The results correspond to the CV% of the control material. The evaluator had no explanation for the difference in some of the duplicate results. The measurements were performed before and after summer holiday and there was no difference before and after. The duplicate measurements from the two comparison method instruments had a CV of <3,0%.

Accuracy of i-CHROMA in primary health care centres

The results are not used for determining accuracy, since some of the samples they originated from were non-centrifuged coagulated whole blood samples, that did not reach the hospital within the day of sampling.

5.5. Evaluation of user-friendliness

5.5.1. *Questionnaire filled in by the evaluators*

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

At the end of the evaluation period, each user filled in a questionnaire about the user friendliness of the instrument. The questionnaire and the expressed opinions are presented in table 21-24. The first column shows what is up for consideration. The second to fourth column show the rating options. The cells with the overall ratings from all three evaluating sites are marked by thicker frames and bold text. The last row in each table summarises the rating in the table. The total rating is an overall assessment of the described property, and not necessarily the arithmetic mean of the rating in the row. Consequently, a single poor rating can justify an overall poor rating, if this property seriously influences on the user-friendliness of the system. Poor ratings are marked with an asterisk and will always be followed by an explanation below the table.

Table 21. Assessment of the information in the manual / insert

Information in the manual / insert	**Red**	**Yellow**	**Green**
General impression	Un-satisfactory	Intermediate	Satisfactory
Table of contents	Un-satisfactory	Intermediate	Satisfactory
Preparations / Pre-analytic procedure	Un-satisfactory	Intermediate	Satisfactory
Specimen collection	Un-satisfactory	Intermediate	Satisfactory
Measurement / Reading	Un-satisfactory	Intermediate	Satisfactory
Measurement principle	Un-satisfactory	Intermediate	Satisfactory
Sources of error	Un-satisfactory	Intermediate	Satisfactory
Fault-tracing / Troubleshooting	Un-satisfactory	Intermediate	Satisfactory
Index*	Un-satisfactory	Intermediate	Satisfactory
Readability / Clarity of presentation	Un-satisfactory	Intermediate**	Satisfactory
Available insert in Danish, Norwegian, Swedish	Un-satisfactory	Intermediate	Satisfactory
Others comments about information in the manual / insert (please specify)	Un-satisfactory	Intermediate	Satisfactory
Rating for the information in the manual			Satisfactory

* The manual has no index, but is very short, and therefore, in SKUP's opinion, does not need one.

Positive comments: -
Negative comments: **The sample guide does not show, that you must squeeze the buffer cup when inserting the sample collector

Table 22. Assessment of time factors

Time factors	**Red**	**Yellow**	**Green**
Time for preparations / Pre-analytical time	>10 min	6 to 10 min.	<6 min.
Analytic time	>20 min	10 to 20 min.	<10 min.
Required training time	>8 hours	2 to 8 hours	<2 hours
Stability of test, unopened package	<3 months	3 to 5 months	>5 months
Stability of test, opened package	<14 days	14 to30 days	>30 days*
Other comments about time factors (please specify)	Un-satisfactory	Intermediate	Satisfactory
Rating of time factors			Satisfactory

*In refrigirator stability is untill expiry date, at room temperature 30 days

Positive comments: -
Negative comments: -

Table 23. Assessment of quality control possibilities

Quality Control	**Red**	**Yellow**	**Green**
Internal quality control	Un-satisfactory	Intermediate	Satisfactory
External quality control	Un-satisfactory	Intermediate	Satisfactory
Stability of quality control material, unopened	<3 months	3 to5 months	>5 months
Stability of quality control material, opened	≤1 day	2 to 6 days	>6 days or disposable
Storage conditions for control materials, unopened	–20°C	+2 to +8°C	+15 to +30°C
Storage conditions for control materials, opened	–20°C	+2 to +8°C	+15 to +30°C
Usefulness of the quality control	Un-satisfactory	Intermediate	Satisfactory
Other comments about quality control (please specify)	Un-satisfactory	Intermediate*	Satisfactory
Rating of quality control		Intermediate**	

Positive comments:
*Negative comments:
- The control was rarely within its range
- Very wide range
- Colourless control material is difficult to see in the blood collector

****'**Intermediate' because the primary health care centres could not use the controls

Table 24. Assessment of the operation facilities

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

Positive comments: - Uses a small sample volume, may be taken in either finger or ear
- Good if you have experienced personnel

Negative comments: - Demands precision and skill, probably not suited for staff without laboratory education

5.5.2. *Assessment of the user-friendliness*

The earlier report SKUP/2008/61 showed good user friendliness despite the fact that the *i*-CHROMA measurement procedure then required more operation step than in this evaluation. The assessment of the operation facilities has been judged differently in this evaluation compared to the earlier evaluations. An experienced biomedical laboratory scientist and two nurses evaluated the user-friendliness of *i*-CHROMA in the report SKUP/2008/61. All three of them had good analytical results with *i*-CHROMA and they all gave the user-friendliness high ratings. They compared *i*-CHROMA with the other near patient P—CRP instruments available. The *i*-CHROMA instrument is now easier to use with fewer operation steps. However, the inexperienced users might not think of the possible pitfalls anymore and then it is easier to make mistakes.

The user must avoid the following mistakes (please look at the pictures in attachment 2):

- Picture 5: When wiping of the sample collector one may accidentally touch the tip of the collector. This can cause less sample volume than required.
- Picture 6: When inserting the sample collector you must squeeze the buffer cup. This is explained in the text, but the picture does not show it. It is important to mix the blood with the buffer in the cup.
- Picture 9: When dripping the two drops from the buffer cup it is important to keep the buffer cup at a distance from the test strip. Otherwise, the squeezed cup may suck up some of the sample material again leaving insufficient sample volume on the test strip.

The evaluation demonstrates that it is possible to achieve good analytical quality with both control samples and blood samples. Two of the evaluators expressed the opinion, that the instrument is best suited for users with laboratory experience.
All the evaluators in this evaluation had less than one hour of training. We think that one hour of training is enough; however, it is essential to pay more attention to avoid mistakes in the measurement procedure when training new users.

The recommended control material is colourless and therefore difficult to handle in the sample collector. In primary health care centre 1, this was shown by poor imprecision achieved with the control material and good imprecision achieved with the patient samples.

6. References

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Additional reading

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Attachments

1. Specifications and basic facts about *i*-CHROMA
2. Guide to sampling (in Danish) used in evaluation
3. New guide to analysing of control material (in Danish)
4. New guide to sampling (in Danish) new
5. Raw data P—CRP, *i*-CHROMA results under standardised and optimal conditions
6. Raw data P—CRP, *i*-CHROMA results from two primary health care centres
7. List of previous SKUP evaluations

Attachments with raw data are included only in the report to Medic24 and Boditech Med Inc.

Attachment 1

Specifications and basic facts about *i*-CHROMA

Table 1. Facts about the measurement system

Name of the measurement system:	*i*-CHROMA CRP Test System
Components of the measurement system:	Capillary blood collector, detector buffer, disposable CRP test strip, *i*-CHROMA reader, System Control strip
Measurand:	P—CRP
Sample material:	EDTA whole blood, capillary whole blood, or plasma/serum
Sample volume:	10 µl
Measuring principle:	Immunoassay with flourescence detection
Traceability:	CRM470
Calibration:	Seven point curve supplied on a chip
Measuring range:	2,5 – 300 mg/L
Linearity:	
Measurement duration:	3 minutes
Operating conditions:	Temperature +15 to +35 ^{o}C

Table 2. Facts about the instrument

Name of the instrument:	*i*-CHROMA reader
Dimensions:	Width: 185 mm Depth: 250 mm Height: 80 mm
Weight:	1,2 kg
Electrical power supply:	AC (100-240 V)
Is input of patient identification number possible?	Yes
Can the instrument be connected to a bar-code reader?	Yes
Can the instrument be connected to a printer?	Yes
What can be printed?	The result of the test with date, time, and test number
Can the instrument be connected to a computer?	Yes
What is the storage capacity of the instrument and what is stored in the instrument?	100 test results with time, date, and test number
Recommended regular maintenance:	Periodic cleaning with a dry cloth
Package contents:	*i*-CHROMA reader, operation manual, power cable, connection cable, System Check Chip set
Necessary equipment not included in the package:	

Table 3. Facts about the reagent/test strips/test cassettes of the measurement system

Name of the reagent/test strips/test cassettes:	*i*-CHROMA CRP Test Kit
Stability in unopened sealed vial:	Test strips: up to 20 months at 2 – 30 ^{o}C Detector buffer: up to 20 monts at 2 – 8 ^{o}C
Stability in opened vial:	Approximately 10 minutes
Package contents:	25 test strips, 25 cups containing detector buffer, ID chip, and 25 blood collection devices

Table 4. Facts about quality control for the measurement system

Electronic self check:	Every time it is turned on and when using the System Check chip
Recommended check materials and volume:	*i*-CHROMA CRP control 10 µl
Stability in unopened sealed vial:	Until expiration date
Stability in opened vial:	One month at 2 – 8 ^{o}C
Package contents:	One vial of *i*-CHROMA CRP control, manual

Table 5. Marketing information about the measurement system

Manufacturer:	BodiTech Med. Inc., 1144-2, Geodu-ri, Dongnae-Myon, Chuncheon, Kangwon-Do, Korea Phone: (+82) 33-243-1400 Fax: (+82) 33-243-9373
Retailers in Scandinavia:	Denmark and Norway: Medic24, Hagebyvegen 40, 3734 Skien, Norway Phone: +47 35570300 Fax: +47 35570301 E-mail: info@medic24.no www.medic24.net Sweden: Medic24 AB, Solvarvsgatan 4, SE-507 40 Borås, Sweden Phone: + 46 33 23 00 99 Fax: + 46 33 23 00 28 E-mail: kundservice@medic24.se www.medic24.se
In which countries is the system marketed:	Globally ☒ Scandinavia ☐ Europe ☐
Date for start of marketing the system in Scandinavia:	2008
Date for CE-marking:	2008
In which Scandinavian languages is the manual available:	Quick guide: Danish, Norwegian, and Swedish

Attachment 2

Patientanalysering

OPBEVARING AF PATIENTPRØVER:

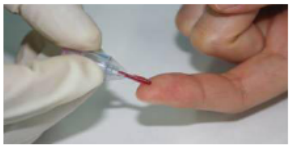
- Prøverøret skal stå på køl i køleskab ved 2-8 °C. Før brug skal prøverøret afklimatiseres i 10 minutter ved stuetemperatur.
- Holdbarheden er 1 uge i stuetemperatur.
- Testkassetter opbevares ved 4-30 °C.
- Hvis kassettene opbevares i kjøleskab, skal de afklimatisere ved stuetemperatur i 10 minutter før anvendelse. Når kassetten er taget ud af folien skal den bruges med det samme.

ANALYSERING AF PATIENTPRØVE:

1 Tænd maskinen og vent til selvtesten af maskinen er godkendt med OK i displayet.

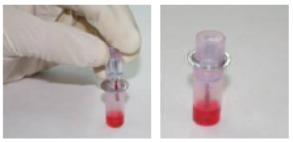
2 Indsæt ID-chippen. Kassetteholderen kommer ud af maskinen og er klar til brug.

3 Bank forsigtig prøveglasset på bænken for å få ev. væske på folien ned. Stik hul i folien til prøveglasset med et nyt kapillærrør.



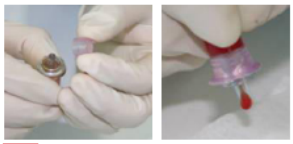
4 Tag en god kapillær prøve med medfølgende kapillær opsamler. Fyld hele kapillæret.

5 Kontroller visuelt, at kapillærrøret er fyldt. Hvis der er blod på ydersiden af kapillærrøret, tørres dette af.

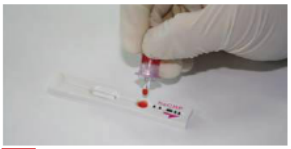


6 Klem prøveglasset med fingrene og sætt kapillærrøret med prøven ned i prøveglasset. Trykk kapillærrøret korrekt ned, mens du slipper klemmingen.

7 Bland grundigt ved at vende hurtig 10 gange.



8 Tag proppen af og dryb først 2 dråber på et stykke papir eller ned i proppen.



9 Dryp 2 dråber på kassetten med det samme.

10 Skub kassetten helt ind i kassetteholderen og tryk Select. Svaret kommer automatisk efter 3 minutter.

11 Efter aflæst svar, tryk Select for at starte ny analyse.

MEDIC 24

MEDIQ DANMARK

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MNA@mediqdanmark.dk

Revideret 23.03.2010

Attachment 3 Guide to analysing of control material (in Danish)

HURTIG-GUIDE i-CHROMA™ Reader

Analyse af kontrol

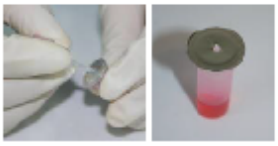
LAGRING AF KONTROLMATERIALE:

- Kontrollen opbevares i køleskab ved 2-8 °C og skal have stuetemp. inden selve analysen.
- Efter brug skal den tilbage i køleskabet , hvorefter holdbarheden er 4 uger i åben tilstand.
- Uåbne kontroller kan anvendes til angivet holdbarhedsdato.
- Værdiene af kontrollen er opgivet i bilag som findes i pakken, samt på kontrolflasken.

ANALYSE AF KONTROL:

1 Tænd maskinen og vent til selvtesten af maskinen er godkendt med OK i displayet.

2 Indsæt ID-chippen og tryk Select. Kassetteholderen kommer ud af maskinen når den er klar til brug.



3 Prik hul i folien på prøveglasset med et nyt kapillærrør.

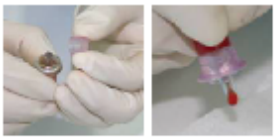
4 Bland stuetempereret kontrol ved at vende flasken flere gange. Pipetter en dråbe af kontrol materiale på evt. folien af kassetten med f.eks. engangs pipette.

5 Fyld en kapillærrør med kontrollmaterialen.

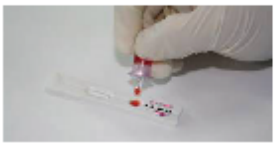
6 Kontrollér visuelt,at kapillærrøret er fyldt. Tør forsigtigt på ydersiden af kapillærrøret.

7 Klem koppen med fingrene og sæt kapillærrøret med kontrollen ned i. Tryk kapillærrøret korrekt ned mens du slipper klemingen.

8 Bland grundigt ved at vende hurtig 10 gange.



9 Tag proppen af og dryp først 2 dråber på et stykke papir eller ned i proppen.



10 Dryp straks 2 dråber på kassetten.

11 Skub kassetten helt ind i kassetteholderen og tryk Select. Svaret kommer automatisk efter 3 minutter.

12 Efter aflæst svar, tryk Select for at starte ny analyse.

Revideret 14.10.2010

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Attachment 4 Guide to sampling (in Danish)

HURTIG-GUIDE i-CHROMA™ Reader

Analysering af patientprøver

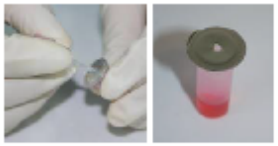
OPBEVARING:

- **Detektor buffer skal opbevares køligt ved 2-8 °C.**
  Før brug afklimatiseres bufferen i 10 minutter ved stuetemperatur.
  Holdbarheden er 1 uge ved stuetemperatur.
- **Testkassetter opbevares ved 4-30 °C.**
  Hvis kassettene opbevares i køleskab, skal de afklimatiseres i 10 minutter ved stuetemperatur før brug. Når kassetten er taget ud af folien skal den bruges med det samme.

ANALYSERING AF PATIENTPRØVE:

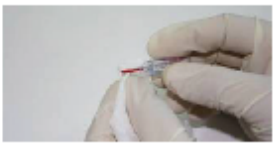
1 Tænd maskinen og vent til selvtesten er godkendt med OK i displayet.

2 Indsæt ID-chippen og tryk Select. Kassetteholderen kommer ud af maskinen og er klar til brug.



3 For at få evt. væske på folien ned i koppen bankes det forsiktig mod bordpladen. Stik hul i folien med et nyt kapillærrør.

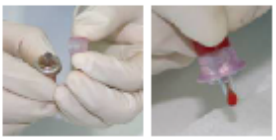
4 Tag en god kapillær prøve med medfølgende kapillærrør. Fyld hele kapillærrøret.



5 Kontrollér visuelt, at kapillærrøret er fyldt. Hvis der er blod på ydersiden af kapillærrøret, tørres dette af.

6 Klem koppen med fingrene og sæt kapillærrøret med prøven ned i . Tryk kapillærrøret korrekt ned mens du slipper klemningen.

7 Bland grundigt ved at vende hurtig 10 gange.



8 Tag proppen af og dryb først 2 dråber på et stykke papir eller ned i proppen.

9 Dryp straks 2 dråber på kassetten.

10 Skub kassetten helt ind i kassetteholderen og tryk Select. Svaret kommer automatisk efter 3 minutter.

11 Efter aflæst svar, tryk Select for at starte ny analyse.

12 For at få kassetteholderen tilbage i instrumentet, skal du trykke på Reset for at komme til MENU bildet og tryk derefter på In/out.

MEDIC 24

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Revideret 14.10.2010

Attachment 5

Raw data P—CRP, *i*-CHROMA results under standardised and optimal conditions

Attachment 6

Raw data Raw data P—CRP, *i*-CHROMA results from two primary health care centres

Attachment 7 List of previous SKUP evaluations

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

SKUP evaluations between 1999 and 2011

Evaluation no.	Component	Instrument/testkit	Producer
SKUP/2010/89*	Glucose	FreeStyle Lite	Abbott Laboratories
SKUP/2010/88	HbA1c	*Confidential*	
SKUP/2011/86	Glucose[1]	OneTouch Verio	LifeScan, Johnson & Johnson
SKUP/2010/82*	Glucose, protein, blood, leukocytes, nitrite	Medi-Test URYXXON Stick 10 urine test strip and URYXXON Relax urine analyser	Macherey-Nagel GmBH & Co. KG
SKUP/2010/81*	Glucose	mylife PURA	Bionime Corporation
SKUP/2010/80	PT (INR)	INRatio2	Alere Inc.
SKUP/2010/79*	Glucose, protein, blood, leukocytes, nitrite	CombiScreen 5SYS Plus urine test strip and CombiScan 100 urine analyser	Analyticon Biotechnologies AG
SKUP/2010/78	HbA1c	In2it	Bio-Rad
SKUP/2009/76*	HbA1c	*Confidential*	
SKUP/2009/75	Glucose	Contour	Bayer HealthCare
SKUP/2009/74	Glucose[1]	Accu-Chec Mobile	Roche Diagnostics
SKUP/2010/73	Leukocytes	HemoCue WBC	HemoCue AB
SKUP/2008/72	Glucose[1]	*Confidential*	
SKUP/2009/71	Glucose[1]	GlucoMen LX	A. Menarini Diagnostics
SKUP/2011/70*	CRP	smartCRP system	Eurolyser Diagnostica GmbH
SKUP/2008/69*	Strep A	Diaquick Strep A test	Dialab GmbH
SKUP/2010/67	Allergens	*Confidential*	
SKUP/2008/66	Glucose[1]	DANA DiabeCare IISG	SOOIL Developement co. Ltd
SKUP/2008/65	HbA1c	Afinion HbA1c	Axis-Shield PoC AS
SKUP/2007/64	Glucose[1]	FreeStyle Lite	Abbott Laboratories
SKUP/2007/63	Glucose[1]	*Confidential*	
SKUP/2007/62*	Strep A	QuikRead	Orion Diagnostica Oy
SKUP/2008/61	CRP	i-CHROMA	BodiTech Med. Inc.
SKUP/2007/60	Glucose[1]	*Confidential*	
SKUP/2007/59	Glucose[1]	Ascensia BREEZE2	Bayer HealthCare
SKUP/2006/58	HbA1c	*Confidential*	
SKUP/2007/57*	PT (INR)	Simple Simon PT	Zafena AB
SKUP/2007/56*	PT (INR)	*Confidential*	

SKUP/2007/55*	PT (INR)	CoaguChek XS	Roche Diagnostics
SKUP/2007/54*	Mononucleosis	*Confidential*	
SKUP/2006/53*	Strep A	*Confidential*	
SKUP/2005/52*	Strep A	Clearview Exact Strep A Dipstick	Applied Biotech, Inc.
SKUP/2005/51*	Glucose[1]	FreeStyle	Abbott Laboratories

SKUP/2006/50	Glucose[1]	Glucocard X-Meter	Arkray, Inc.
SKUP/2006/49	Glucose[1]	Precision Xtra Plus	Abbott Laboratories
SKUP/2006/48	Glucose[1]	Accu-Chek Sensor	Roche Diagnostic
SKUP/2006/47	Haematology	Chempaq XBC	Chempaq
SKUP/2005/46*	PT (INR)	*Confidential*	
SKUP/2006/45	Glucose[1]	HemoCue Monitor	HemoCue AB
SKUP/2005/44	Glucose[1]	Accu-Chek Aviva	Roche Diagnostics
SKUP/2005/43	Glucose[1]	Accu-Chek Compact Plus	Roche Diagnostics
SKUP/2005/42*	Strep A	Twister Quick-Check Strep A	ACON laboratories, Inc.
SKUP/2006/41*	HbA1c	*Confidential*	
SKUP/2005/40	Glucose[1]	OneTouch GlucoTouch	LifeScan, Johnson &
SKUP/2005/39	Glucose[1]	OneTouch Ultra	LifeScan, Johnson &
SKUP/2004/38*	Glucose	GlucoSure Plus	Apex Biotechnology
SKUP/2004/37*	u-hCG	Quick response u-hCG	Wondsfo Biotech
SKUP/2004/36*	Strep A	Dtec Strep A testcard	UltiMed
SKUP/2004/35*	u-hCG	RapidVue u-hCG	Quidel Corporation
SKUP/2004/34*	u-hCG	QuickVue u-hCG	Quidel Corporation
SKUP/2004/33	PT (INR)	Hemochron Jr. Signature	ITC International
SKUP/2004/32*	Strep A	QuickVue In-Line Strep A test	Quidel Corporation
SKUP/2004/31*	PT (INR)	*Confidential*	
SKUP/2004/30	Glucose[1]	Ascensia Contour	Bayer Healthcare
SKUP/2004/29	Haemoglobin	Hemo Control	EKF-diagnostic
SKUP/2003/28*	Strep A	QuickVue In-Line Strep A test	Quidel Corporation
SKUP/2003/27*	Strep A	QuickVue Dipstick Strep A test	Quidel Corporation
SKUP/2003/26*	HbA1c	*Confidential*	
SKUP/2003/25*	HbA1c	*Confidential*	
SKUP/2003/24*	Strep A	OSOM Strep A test	GenZyme, General Diag.
SKUP/2002/23*	Haematology with CRP	ABX Micros CRP	ABX Diagnostics
SKUP/2002/22	Glucose[1]	GlucoMen Glycó	Menarini Diagnostics
SKUP/2002/21	Glucose[1]	FreeStyle	TheraSense Inc.
SKUP/2002/20	Glucose	HemoCue 201	HemoCue AB
SKUP/2002/19*	PT(INR)	Reagents and calibrators	
SKUP/2002/18	Urine– Albumin	HemoCue	HemoCue AB
SKUP/2001/17	Haemoglobin	Biotest Hb	Biotest Medizin-technik GmbH
SKUP/2001/16*	Urine test strip	Aution Sticks and PocketChem UA	Arkray Factory Inc.
SKUP/2001/15*	Glucose	GlucoSure	Apex Biotechnology Corp.
SKUP/2001/14	Glucose	Precision Xtra	Medisense
SKUP/2001/13	SR	Microsed SR-system	ELECTA-LAB

SKUP/2001/12	CRP	QuikRead CRP	Orion
SKUP/2000/11	PT(INR)	ProTime	ITC International Technidyne Corp
SKUP/2000/10	PT(INR)	AvoSure PT	Avocet Medical Inc.
SKUP/2000/9	PT(INR)	Rapidpoint Coag	
SKUP/2000/8*	PT(INR)	Thrombotest/Thrombotrack	Axis-Shield
SKUP/2000/7	PT(INR)	CoaguChek S	Roche Diagnostics
SKUP/2000/6	Haematology	Sysmex KX-21	Sysmex Medical Electronics Co
SKUP/2000/5	Glucose	Accu-Chek Plus	Roche Diagnostics
SKUP/1999/4	HbA1c	DCA 2000	Bayer
SKUP/1999/3	HbA1c	NycoCard HbA1c	Axis-Shield PoC AS
SKUP/1999/2*	Glucose	Precision QID/Precision Plus Electrode, whole blood calibration	Medisense
SKUP/1999/1	Glucose	Precision G/Precision Plus Electrode, plasma calibration	Medisense

*A report code followed by an asterisk, indicates evaluations at special request from the supplier, or evaluations that are not complete according to SKUP guidelines, e.g. the part performed by the intended users was not included in the protocol.

[1] Including a user-evaluation among diabetes patients

Grey area – The instrument is not in the Scandinavian market any more

Attachment 8

Dr. Esther Jensen

SKUP in Denmark

Deres ref: Esther Jensen | Vår ref: Helena Olkkonen-Ure | Dato: 2011-09-06

Comments from Medic24 AS to SKUP report nr. 90

Thank you for performing the evaluation of i-CHROMA CRP. The report shows that i-CHROMA CRP method is indeed a good system when the tests are performed correctly. Between the time period of when this evaluation was started and until this date, several of the "pitfalls" mentioned in the report have been corrected already. Here is the a list of changes that have already been effectuated or will be in September 2011.

1. The buffer reagent is stable in opened package up to ext. date in case kept in refrigerator, 1 month in room temperature (page 36).
2. The sample guide has been changed after the SKUP evaluation started. At the present sample guide (revised 14.10.2010) there is picture and text that shows that the buffer cup should be squeezed when inserting the sample collector (page 35).
3. There have already since March 2011 been a new control at the market with a pink colour. This change makes it easier to use the controls. The new control that has come in August 2011 have even more red colour and it is stable for 3 months after it has been opened. There is a new control coming in 2012 with a drop bottle and extended stability (page 37).
4. At page 36 in table 21 there is a comment nr. 2 about the squeezing of the buffer cup. The mixing of the buffer cup is clearly told in the revised sample guide. Dripping of the two drops to the cartridge from the distance is shown with picture.
5. There is already planned a new rev. of the sample guide due in September 2011 with following changes: a text that says that there must be "hanging drops" when dripping to the cartridge, 1 month in room temperature for the buffer reagents, 3 months of stability for new control after opening.

Yours sincerely

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