CombiScreen 5SYS Plus and CombiScan 100

A urine test strip and urine analyser
from Analyticon Biotechnologies AG

Report from an evaluation
organised by SKUP

The evaluation was ordered by Medinor ASA, Norway

SKUP/2010/79*

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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 organising 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.

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

[2] SKUP in Denmark is placed in 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.

The report is written by
SKUP in Norway,
May 2010

1. Summary

Background
Urine test strips are used as a screening method for early detection of possible diseases such as metabolic disorders, diseases of the kidneys and urogenital tract, and liver and haemolytic diseases. The urine test strip CombiScreen 5SYS Plus and the urine analyser CombiScan 100 are produced by Analyticon Biotechnologies AG and supplied in Scandinavia by Medinor. The system has not been launched onto the Scandinavian market yet. A pre-evaluation of CombiScreen 5SYS Plus and CombiScan 100 was carried out under the direction of SKUP from November 2009 to March 2010. The urine test strip contains test pads for glucose, protein, blood, nitrite and leukocytes.

The aim of the evaluation
The aim of the evaluation of CombiScreen and CombiScan is to

- reflect the analytical quality under standardised and optimal conditions, performed by a biomedical laboratory scientist in a hospital environment
- compare the analytical quality between visual and mechanical reading of CombiScreen 5SYS Plus
- compare the analytical quality with two of the market leading products for urine analysis in Norway:
  - ✓ Clinitek Status+ Analyser (Siemens) with Multistix 8 SG urine test strip
  - ✓ Urisys 1100 Analyser (Roche) with Combur^{5} Test urine test strip
- evaluate the system regarding user-friendliness

Materials and methods
This evaluation is a rating agreement study performed between CombiScreen 5SYS Plus and two of the market leading products in Norway for analysing of urine samples with test strips. The evaluation took place at NOKLUS in Bergen. Urine samples were collected from the laboratory and the emergency care unit at Haraldsplass Diaconale Hospital, the Laboratory of Clinical Biochemistry at Haukeland University Hospital and at Volvat Medical Centre in Bergen. The aim was to collect 100 positive urine samples for each of the components leukocytes, protein and nitrite. The samples were stored in the fridge until they were analysed at NOKLUS within 24 hours after sample collection. Two CombiScreen 5SYS Plus test strips, one Combur^{5} Test and one Multistix 8 SG test strip were immersed in each urine sample. Visual reading of CombiScreen 5SYS Plus was carried out before the mechanical reading of a new test strip on CombiScan 100. The three analysers read the urine samples in succession in the following reading order: CombiScan 100, Urisys 1100 and Clinitek Status+. Rating agreement analysis can never give true information about the analytical quality of the instrument. A reasonable use of the agreement data is to interpret the revealed agreement or disagreement as follows: If two raters disagree, at least one of them must be *incorrect*. If the raters agree, the next step should be to document if they are correct.
Daily maintenance of the three analysers was carried out prior to starting the daily analysis. The user-friendliness of CombiScan 100 was assessed.

Results
The agreement was good between visual and mechanical reading of CombiScreen 5SYS Plus for the component nitrite with a kappa coefficient (κ) >0,8. The agreement was acceptable[4] for the components glucose, protein and blood with κ≥0,6. There was a disagreement between visual and mechanical reading for the component leukocytes. The κ_{max} score for leukocytes of 0,64 verifies that there was an underlying bias between visual and mechanical reading for this component.

The agreement was good between CombiScan 100 and Clinitek Status+ for the components glucose, leukocytes and nitrite with κ>0,8. The agreement was acceptable for the component blood.

When CombiScan 100 was compared to Urisys 1100, nitrite showed good agreement and glucose showed an acceptable agreement. For the components blood and leukocytes the κ_{max} score was 0,68 and 0,76 respectively, and verifies that there was a discrepancy between CombiScan 100 and Urisys 1100 for these two components.

For the component protein a low κ and κ_{max} score indicate a disagreement between all three urine analyzers. The results must be compared to a quantitative method for determination of protein in urine to find which method that lies closest to the true value.

The different agreement of CombiScan 100 and the two comparison methods is caused by a certain deviation between the two comparison methods.

The CombiScan system was regarded as user-friendly.

Conclusion
Visual and mechanical reading of CombiScreen 5SYS Plus: The agreement was good for the component nitrite, and acceptable for the components glucose, protein and blood. There was a disagreement for the component leukocytes.

A certain deviation between the two comparison methods was observed during the evaluation, most pronounced for the component protein. This explains a different agreement between CombiScan 100 and the two comparison methods in this evaluation.
Comparison with Clinitek Status+: The agreement was good for the components glucose, leukocytes and nitrite, and acceptable for the component blood. There was a disagreement for the component protein.
Comparison with Urisys 1100: The agreement was good for the component nitrite and acceptable for the component glucose. There was a disagreement for the components blood, leukocytes and protein.
User-friendliness: The CombiScan system was regarded as user-friendly.

Comments from Analyticon
A letter with comments from Analyticon Biotechnologies AG is attached to the report. Please see attachment 9.

[4] Kappa coefficients between 0,60 and 0,80 were described as acceptable. Agreement in this intermediate category is neither good nor bad.

2. Analytical quality goals

Qualitative and semi-quantitative measurements are often expressed as categorical data and can be read on the ordinal scale; an example of this is the reading of urine test strips in arbitrary units. When comparing methods read on the ordinal scale, it is practical to use Concordance analysis with Kappa statistics [1] [2]. The aim of the model is to decide on the agreement between two or more ordinal scale categories based on contingency tables of two or more classes (e.g. 2 x 2, 3 x 3 tables, etc.). In the majority of cases, the diagonal in the tables will represent correlated/corresponding observations between the methods. For more details about Kappa statistics, se chapter 4 “Statistical expressions and calculations”.

Requirements set for the assessment of the Kappa value are based on the fact that semi-quantitative studies will classify more than half of the cases not due to chance as correct [1].

Analytical quality specifications expressed as Cohen’s Kappa coefficient (κ).

	Optimum	**Minimum**
Simple κ coefficient	>0.8	>0.6

The quality specifications are based on common sense: any clinical laboratory examination should classify more than half of the non-random cases correctly. Arbitrarily, this is equivalent to κ>0,6, although optimally the value should be >0,8 if achievable.

The Kappa coefficient will be provided with a 95% confidence interval, calculated using the standard error of κ.

3. Materials and methods

3.1. CombiScreen 5SYS Plus and CombiScan 100

3.1.1. CombiScreen 5SYS Plus urine test strip

The CombiScreen 5 SYS Plus urine test strip used in this evaluation is produced by Analyticon, and contains test pads for glucose, protein, blood, nitrite and leukocytes. The test pads for blood and glucose have a protection against interferences caused by ascorbic acid. The urine test strips should be stored in the test strip box at temperatures between 2 and 30°C and have a shelf life that equates to the expiry date specified on the box. The test strips can be used for visual readings or for mechanised reflectance-photometric evaluations. Immersion time in urine is approximately two seconds. The urine test strip should be read after 60 seconds for glucose, protein, blood and nitrite, and after 60 - 120 seconds for leukocytes.

<u>The principle for the test pads on the CombiScreen 5SYS Plus test strip:</u>

Glucose

Detection of glucose in the urine is based on a glucose oxidase (GOD) - peroxidase (POD) - chromogen reaction (green-blue colour reaction). Colorations weaker than the pad for 2,8 mmol/L, should be classified as normal.

$$\text{Glucose} + O_2 \xrightarrow{\text{GOD}} \text{Gluconolactone} + H_2O_2$$

$$\text{Chromogen} + H_2O_2 \xrightarrow{\text{POD}} H_2O + \text{dye}$$

Protein

The test pad reacts particularly sensitively to albumin. The test is based on the "protein error" principle of the indicator that changes colour from yellow to green. A colour reaction is observed from 0,15 g/L albumin.

$$\text{Indicator dye (yellow)} \xrightarrow[-H^+]{\text{Protein}} \text{Indicator dye anion (green)}$$

Blood

The test pad detects occult blood in urine. This test is based on the peroxidative activity of haemoglobin and myoglobin (green colour reaction). Intact erythrocytes lyses on the pad. The haemoglobin released by the cells causes a change in colour; visible green dots appear in the surroundings of the erythrocytes. The haemoglobin dissolved in the urine (lysed erythrocytes) gives a homogeneous green colour.

$$\text{Organic Hydroperoxide} + \text{Haemoglobin} + \text{Chromoge} \longrightarrow \text{Organic Hydroxy compound} + \text{dye}$$

The visual reading of blood can be registered in two ways; intact erythrocytes are reported by green dots on the test pad, whereas hemoglobin and myoglobin (lysed erythrocytes) are reported by a homogenous green colour. The mechanical detection of blood is independent of whether the green colour is present in dots, in a homogenous colour or in a mix of both.

Leukocytes
Detection of leukocytes is based on the activity of esterase from granulocytes which gives a violet colour reaction on the test pad.

Indoxylester $\xrightarrow{\text{Esterase}}$ Indoxyl

Indoxyl + diazonium salt $\longrightarrow$ dye (violet)

Nitrite
Nitrite detection is specific for detecting bacteriuria. The detection limit for nitrite is given at 0,05 – 0,1 mg/dL (6,5 - 13 µmol/L). According to the package insert of the CombiScreen test strip, >90% of the results for nitrite are showing positive results for visual evaluation at the detection limit. The test is based on the Griess reaction (pink colour reaction). Any degree of pink coloration should be interpreted as a positive nitrite test, suggestive of $\geq 10^5$ bacteria per mL urine.

Nitrate $\xrightarrow{\text{Bacterial reduction in urine}}$ nitrite

Nitrite + aromatic amine $\xrightarrow{H^+}$ diazonium salt

diazonium salt + coupling components $\longrightarrow$ Azo dye (red)

When checking for nitrite, the sample must be the first morning urine, or the urine should have been in the bladder for a minimum of four hours before taking the sample. We disregarded this guideline in the evaluation because we did not search for the "true" patient result, but assessed the agreement between the different types of urine test strips. The detection limit for nitrite is given at 0,05 mg/dL (11 µmol/L) for the comparison method Combur^5 Test (Roche) and 0,06 mg/dL for Multistix 8 SG (Siemens).

3.1.2. CombiScan 100 Urine Analyser

The CombiScan 100 Analyser is a semi-automated system and the measurement principle is reflectance photometry. CCD (Charge-Coupled-Device) technology is used to analyse colour development and light intensity reflected from the surface of the different test pads. The CCD technology provides the analyser to distinguish between coloration caused by a reaction with test pad chemicals and non-specific coloration caused by the urine sample. The CombiScan 100 can carry out 120 tests per hour in "Fast mode", assuming that the user carries out an incubation period of 60 seconds before the test strip is read in the analyser. The capacity is 40 tests per hour in "Normal mode", as the test strip is incubated in the analyser before it is read. Most users are running the analyzer in the normal mode. For that reason, the normal mode was used during this evaluation.

The analyser can store 460 test results; 460 patient results or 400 patient results and 30 QC-results of a 2-level control if the lockout-mode is activated. A "check test holder" is used to check the analyser's optics.

More facts about the system are shown in attachment 1.

3.1.3. Product information

For manufacturer of the system and suppliers in the Scandinavian countries, see attachment 1.

CombiScan 100
Serial no. 204849

CombiScreen 5SYS Plus urine test strip
Lot A, lot no. 6427/7006 Exp. 2011/10
Lot B, lot no. 6428/7014 Exp. 2011/10
Lot C, lot no. 6429/7021 Exp. 2011/10

CombiScreen Control PN (level P, level N)
Lot no. 6418/1054 Exp. 2011/01

3.2. Designated comparison method

A designated comparison method is a fully specified method which, in the absence of a Reference method, serves as the common basis for the comparison of a field method.

3.2.1. The comparison methods in this evaluation

An agreement study is an indirect attempt to validate a new rating system or instrument. Because of the lack of a definitive criterion variable or "gold standard", and lack of an accessible designated comparison method, the accuracy of the new system is assessed by comparing its results with results from similar raters. In this evaluation it was decided to compare the CombiScan system with two of the market leading products for reading of urine samples in Norway.

Multistix 8 SG urine test strip and Clinitek Status+ Analyser
The urine test strip and the analyser are manufactured by Siemens. The test strip contains test pads for glucose, protein, blood, nitrite, leukocytes, pH, specific gravity and ketones. Specific gravity, pH and ketones are not part of the evaluation. The test principles for the test pads included in the evaluation, are the same as those for CombiScreen 5SYS Plus or similar. Maximum immersion time in urine is approximately one second. The measurement principle in Clinitek Status+ is reflectance photometry.

Combur^{5} Test urine test strip and Urisys 1100 Analyser
The urine test strip and the analyser are manufactured by Roche. The test strip contains test pads for glucose, protein, blood, nitrite and leukocytes. The test principles are the same as those for CombiScreen 5SYS Plus or similar. Maximum immersion time in urine is approximately one second. The measurement principle in the Urisys 1100 is reflectance photometry.

3.2.2. Verification of the analytical quality of the comparison methods

Daily maintenance of Urisys 1100 and Clinitek Status+ was carried out prior to starting the daily analysis. At start-up, an automatic optical test is carried out on both analysers. Afterwards analysis of the manufacturers' urine control solutions at two levels was carried out. The results were entered on a separate form, see chapter 5.1.

3.2.3. Product information, the comparison methods

Analyser

Roche:	Urisys 1100	Serial no. UX09623814	
Siemens:	Clinitek Status+	Serial no. 200265	

Urine test strip

Roche:	Combur^{5} Test	Lot no. 23052245	Exp. 2010/11
Siemens:	Multistix 8 SG	Lot no. 9G25C	Exp. 2011/01
		Lot no. 9J11DC	Exp. 2011/02

Internal quality control
Quantimetrix the Dipper, Urine dipstick control 1&2 (used for the Roche system)
Lot no. 44490K Exp. 2010/08
Siemens Chek-Stix Combo Pak Control +/-
Lot no. C0071079E Exp. 2011/01

3.3. Planning of the evaluation

Background for the evaluation

CombiScreen Urine test strips are used as a screening method for early detection of possible diseases such as metabolic disorders, diseases of the kidneys and urogenital tract, and liver and haemolytic diseases. The test strips can be used for mechanised reflectance-photometric evaluations. Urine test strips are routinely used in primary healthcare centres, in hospital laboratories and for bedside testing. The CombiScreen 5SYS Plus and CombiScan 100 is produced by Analyticon Biothechnologies AG and supplied in Scandinavia by Medinor. The system has not been launched onto the Scandinavian market yet. Medinor in Norway turned to SKUP in March 2009 with an enquiry about a pre-evaluation of CombiScreen 5SYS Plus urine test strip and the CombiScan 100 urine analyser. They wanted an assessment of the analytical quality of the system. Two of the market leading products for urine analysis in Norway, the systems from Roche and Siemens, were selected to be the comparison methods.

Contract, protocol and arrangements

Sølvi Haga from Medinor and Klaus Langer and Tomas Blomquist from Analyticon came to SKUP for a meeting in June 2009. The arrangement for an evaluation was agreed upon, and SKUP offered to start the evaluation during autumn 2009. SKUP made a proposal for an evaluation protocol in September 2009. The protocol was approved in November and the evaluation contract was signed.

Preparations and training program

The preparations for the evaluation started in September 2009. Sonja Lauterbach from Analyticon came to SKUP in November to give practical training in use of the urine system to Grete Monsen and Camilla Eide Jacobsen. SKUP received all the equipment for the evaluation from Analyticon in November.

Collection of the urine samples

The practical work with the evaluation was carried out from November 2009 to March 2010. Urine samples were collected from the laboratory and the emergency care unit at Haraldsplass Diaconale Hospital, the Laboratory of Clinical Biochemistry at Haukeland University Hospital and at Volvat Medical Centre in Bergen. Once the laboratories had analysed the urine samples according to their routine procedures, the samples were stored in the fridge until they were analysed at NOKLUS.

3.3.1. Evaluation sites and persons involved

The evaluation took place at NOKLUS in Bergen. Grete Monsen, SKUP, was the contact person and was responsible for the evaluation. Biomedical laboratory scientist, Camilla Eide Jacobsen, was responsible for the practical work. The Laboratory of Clinical Biochemistry and Volvat Medical Centre were contacted by advisory biomedical laboratory scientists Stein Binder and Hilde-Kristin Rondestveit, NOKLUS. Urine samples from these two laboratories were collected by Hilde-Kristin and Stein. Camilla had the responsibility to collect urine samples from the laboratory and the emergency care unit at Haraldsplass Diaconale Hospital. The statistical calculations are done by Camilla Eide Jacobsen, and the report is written by Camilla Eide Jacobsen and Grete Monsen.

3.4. The evaluation procedure

3.4.1. The model for the evaluation of CombiScreen 5SYS Plus and CombiScan 100

The SKUP evaluation

The evaluation is carried out under the auspices of SKUP and follows to some extent the fundamental guidelines in the book "*Evaluation of analytical instruments. A guide particularly designed for evaluations of instruments in primary health care*" published by Alma Mater Forlag in autumn 1997 (ISBN 82-419-0230-1) [3].

This evaluation is a rating agreement study. The evaluation of CombiScreen 5SYS Plus and CombiScan 100 comprises the assessment of the analytical quality under standardised and optimal conditions, performed by a biomedical laboratory scientist in a laboratory environment. This includes:

- a comparison between visual and mechanical reading of CombiScreen 5SYS Plus
- a comparison with two of the market leading products for urine analysis in Norway:
  - the Clinitek Status+ Analyser (Siemens) with the Multistix 8 SG urine test strip
  - the Urisys1100 Analyser (Roche) with the Combur^5 Test urine test strip
- evaluation of user-friendliness

Training

Training in the use of the CombiScan 100 analyser was provided by Sonja Lauterbach from Analyticon. The biomedical laboratory scientist spent sufficient time familiarising herself with the analyser before the start of the evaluation.

3.4.2. Handling of the urine samples and test strips

Handling of the urine samples

In the evaluation protocol it was suggested to aim at collecting 100 positive urine samples for each of the components leukocytes, protein and nitrite. To be counted as a positive sample it was enough with a positive reaction on one of the three systems. To achieve results throughout the whole glucose measuring range, it became necessary to produce some urine samples by adding glucose to "normal" urine samples. All urine samples were kept in the fridge at NOKLUS until they were analysed for the evaluation. Storage-time of the urine samples was not critical, since the reading of each sample with the different methods was done consecutively and within 2 minutes. The urine samples were analysed within 24 hours after sample collection, and the samples achieved room temperature and were mixed prior to analysis.

Handling of the urine test strips

The urine test strips were kept in the test strip box until they were used. The box was closed immediately after the test strip had been removed. The boxes were stored at room temperature between 20 and 25°C and were used within the expiry date. All instructions in the user's manual and in the package insert were followed closely.

Immersion of urine test strips in urine

The immersion time in urine was two seconds for CombiScreen 5SYS Plus and one second for each of the test strips Combur^5 Test and Multistix 8 SG. After the immersion of the test strip in the urine, the strip was held horizontally to avoid reagent contamination. Excess urine on the test strip was removed by touching the side edge of the test strip against a piece of absorbent paper. Some urine samples were kept in the original containers, and some were transferred to a more

practical container for dipping of the test strip. Two CombiScreen 5SYS Plus test strips, one Combur[5] Test and one Multistix 8 SG test strip were immersed in each urine sample. In addition, a test strip had already been immersed in the urine container at the laboratory where the urine sample was collected. In total, five urine test strips were immersed per urine sample.

Restrictions on the number of immersions per urine sample
Analyticon states that up to ten test strips may be immersed in the same urine without this having an effect on the results. Bayer states that 10–12 test strips may be immersed in the same urine control solution without this affecting the results and concludes that this also applies to urine samples. Roche states that up to ten test strips may be immersed in urine where the volume of urine sample is at least 10 mL.

3.4.3. Visual reading of urine test strips

Only the CombiScreen 5SYS Plus urine test strip was read visually. Visual reading was carried out before the mechanical reading with CombiScan 100, so that the result of the visual reading was not influenced by the result from the analyser. A stopwatch was used. The reaction time for CombiScreen 5SYS Plus is 60 seconds for glucose, protein, blood and nitrite and 60-120 seconds for leukocytes. Colours of leukocytes test pad that cannot be clearly assigned to negative or 1+ after 60 seconds can be assigned more clearly at 120 seconds. Coloration after 120 seconds was not read. The urine test strip was compared with the colour codes on the test strip box and the results were read in the order shown on the box. The coloration of the test pad was read against the colour code on the test strip box that was closest to the colour in the reaction. The visual evaluation of CombiScreen 5SYS Plus was performed in a small laboratory with good lighting, approved by Sonja Lauterbach from Analyticon. The results were recorded on the result form prepared by SKUP.

3.4.4. Mechanical reading of urine test strips

The analysers used in the evaluation was the CombiScan 100 Analyser with the CombiScreen 5SYS Plus urine test strip, the Urisys1100 analyser with the Combur[5] Test urine test strip and the Clinitek Status+ Analyser with the Multistix 8 SG urine test strip. All three analysers have built-in printers. The results were recorded on the result form prepared by SKUP and all original printouts were kept.

3.4.5. Analysing procedure

The urine sample was brought to room temperature and mixed prior to analysis. The colour of the urine was noted on the result form (clear, pale yellow, yellow, dark yellow or brown). The four urine test strips were read in succession mentioned below. The readings for each sample were carried out within 2 minutes.

- Urine test strip 1: CombiScreen 5SYS Plus, visual reading
- Urine test strip 2: CombiScreen 5SYS Plus, mechanical reading with CombiScan 100
- Urine test strip 3: Combur[5] Test, mechanical reading with Urisys 1100
- Urine test strip 4: Multistix 8 SG, mechanical reading with Clinitek Status+

For information about immersion of urine test strips in urine and mechanical reading of urine test strips, see section 3.4.2 and 3.4.4.

3.4.6. Maintenance and quality control of the analysers

Daily maintenance of all three analysers was carried out prior to starting the daily analysis. Before analysing the CombiScreen control PN urine control (two levels), an optical test was carried out on the CombiScan 100 by analysing the "check test strip holder". The results were entered on a separate form. For the two comparison methods, the urine quality controls recommended by the manufacturers were analysed before starting the daily analysis, see section 3.2.2.

3.4.7. Registration of results

All results were registered consecutively by the biomedical laboratory scientist carrying out the practical work. A registration form adapted for this evaluation was used (prepared by SKUP). Raw data will be attached to the final report that is sent to Analyticon and Medinor, but will not be attached to the published report.

3.4.8. Evaluation of user-friendliness

Once the practical work was carried out, the user-friendliness of CombiScan 100 was evaluated by the biomedical laboratory scientist. The evaluation form prepared by SKUP was used, see chapter 5.5.

4. Statistical expressions and calculations

4.1. Statistical terms and expressions

4.1.1. Concordance analysis with kappa statistics

Kappa statistics was used to calculate the degree of agreement. The kappa model takes into account the fact that two methods may agree by chance. The agreement that may occur by chance is calculated and deducted from the observed data. The calculated Cohen's Kappa coefficient (κ) is a measure of the degree of agreement between the methods that are being compared.

Simple kappa statistics are primarily used when there are only two or three categories to compare. Weighted kappa is used for contingency tables above a particular number of categories (4–5 classes) where the extent of the difference between the two methods being compared is taken into consideration. The categories are weighted according to where they are in relation to the category where it is expected that the methods agree. Weighted kappa penalizes disagreement in terms of their seriousness, whereas un-weighted kappa treats all disagreements equally [4]. In the evaluation the agreement between the methods for the components glucose, protein, blood and leukocytes will be calculated using weighted kappa, attaching greater emphasis to large differences between ratings than to small differences. Un-weighted kappa will be used for the calculation of agreement for nitrite.

It is suggested that the interpretation of kappa is assisted by also reporting the maximum value kappa can attain for the set of data concerned (κ_{max}) [4]. For a given reliability study, the difference between kappa and 1 indicates the total unachieved agreement beyond chance. The difference between κ_{max} and 1 shows the effect on agreement of imbalance in the table totals, caused by pre-existing factors such as method bias. This provides useful information [4]. For the calculation of kappa and maximum kappa, see section 4.2.

Kappa statistics can only be used on symmetrical tables, e.g. 2 x 2, 5 x 5 etc. In this evaluation most of the tables have different numbers of columns and rows (e.g. 4 x 5 etc.). When calculating the kappa coefficient, these tables will have two rows or columns combined where one of the methods has an answer alternative more than the other method. The conversion from an asymmetrical table to a symmetrical table is illustrated in attachment 2.

4.1.2. Overall agreement

The calculation of overall agreement between the methods is performed to show accordance independent of the categorisation of the methods.

4.2. Statistical calculations

4.2.1. Number of samples

201 urine samples were collected for the analysis of glucose, protein, erythrocytes, leukocytes and nitrite. In addition 10 urine samples for analysis of glucose were made at NOKLUS by adding different concentrations of glucose to a "normal" urine sample. In addition, 44 urine samples were collected specially for the analysis of nitrite. There are no missing or excluded results in this evaluation.

4.2.2. Calculation of Cohen's Kappa coefficient

Calculation of the Kappa coefficient [1]: **$\kappa = (Po - Pe)/(1 - Pe)$**, where

Po = observed probability of agreement
Pe = expected probability of agreement by chance
(1 – Pe) = expected disagreement by chance

Kappa has the value of 1 when there is perfect agreement between the methods. A value of zero indicates that possible agreement of the two methods only occurs by chance. An un-weighted kappa value does not distinguish between the magnitudes of disagreement on samples.

4.2.3. Calculation of weighted kappa

The weights can be assigned by means of any judgement procedure set up to reflect the results on a ratio scale. The weights may be the result of a consensus of experts, or they can simply be the investigator's own judgement. The choice of weights will obviously affect the resulting kappa values, and can therefore be decisive for the assessments and conclusions.

In this evaluation it was decided to use the Fleiss-Cohen quadratic weights [4,5] in calculation of the weighted kappa coefficient. Fleiss-Cohen weights are based on agreement. In the evaluation the method of weighting is based on disagreement, where the magnitude of discrepancy is indicated in the weight given each pair of observations. This method of weighting will give a low value of kappa when methods have a large discrepancy between ratings. The magnitude of the weights used in this evaluation is quite moderate with a maximum weighting of 2,00. Illustration of the quadratic weights used in cross-tables 6x6 and 4x4 are presented in figure 1.

Answer alternatives	Weights					
	1	2	3	4	5	6
1	1,00	1,04	1,16	1,36	1,64	2,00
2	1,04	1,00	1,04	1,16	1,36	1,64
3	1,16	1,04	1,00	1,04	1,16	1,36
4	1,36	1,16	1,04	1,00	1,04	1,16
5	1,64	1,36	1,16	1,04	1,00	1,04
6	2,00	1,64	1,36	1,16	1,04	1,00

Answer alternatives	Weights			
	1	2	3	4
1	1,00	1,11	1,44	2,00
2	1,11	1,00	1,11	1,44
3	1,44	1,11	1,00	1,11
4	2,00	1,44	1,11	1,00

Figure 1. Illustration of quadratic weights inn cross-tables 6x6 and 4x4

4.2.4. Calculation of maximum kappa (κ_{max})

To calculate the maximum attainable kappa (κ_{max}), the proportions of judgments by each rater (i.e., the table totals) are taken as fixed. The distribution of paired ratings is then adjusted so as to represent the greatest possible agreement. κ_{max} serves to gauge the strength of agreement while preserving the proportions of positive ratings demonstrated by each rater [4].

4.2.5. Assessment of the kappa coefficient

There is no general opinion on how to assess kappa coefficients for comparisons of urine test strips. In this evaluation a Kappa coefficient >0,80 was assessed as good agreement between the methods. A Kappa coefficient <0,60 was assessed as a disagreement. Kappa coefficients between 0,60 and 0,80 were described as acceptable. The agreement in this intermediate category is neither good nor bad. SKUP will probably use a more neutral term than acceptable for agreement according to this intermediate category in later evaluations of urine test strips.

4.2.6. Calculation of overall agreement

To calculate the overall agreement between the methods, the total number of concurrent results is divided with the overall number of results, and the answer is given in percent. The answer is provided with a 95% confidence interval based on binomial distribution.

5. Results and discussion

5.1. Internal quality control

The internal quality control measurements on Urisys 1100 were performed with Urine dipstick control Quantimetrix the Dipper 1&2 (negative and positive level). The internal quality control measurements on Clinitek Status+ were performed with Chek-Stik Combo Pak Control +/-. The internal quality control measurements on CombiScan 100 were performed with CombiScreen Control PN (negative and positive level). All control measurements were performed daily by the biomedical laboratory scientist throughout the evaluation period. The control solutions were kept according to the instructions in the product inserts. The expiring time after opening was not exceeded. An optical test was performed at each system before analysing the controls. All of the optical tests passed during the whole evaluation period.

The results of the internal quality controls on the three systems were inside the limits stated by the producer of the control solutions. The raw data from the measurements with internal quality control solutions is shown in attachment 3 and 4.

5.2. Assessment of analytical quality

Rating agreement analysis can never give true information about the analytical quality of an instrument. A reasonable use of the agreement data is to interpret the revealed agreement or disagreement as follows: If two raters disagree, at least one of them must be *incorrect*. If the raters agree, the next step should be to document if they are correct.

Cross-tables are made to illustrate the agreement between visual and mechanical readings of CombiScreen 5SYS Plus, and between mechanical readings at CombiScan 100 and the two comparison methods; Urisys 1100 and Clinitek Status+. The coloured areas in the tables (purple) represent the correlated/corresponding observations between the methods. For assessment of the agreement with the two comparison methods in section 5.4, the coloured areas in the tables (purple) are based on visual inspection of the transitional points (cut-offs) in figure 2 to 5. The theoretical cut-off between two subsequent answer alternatives is suggested as the mean of the given concentration for the two alternatives.
In some of the tables one of the methods has an answer alternative that covers two answer alternatives of the other method (illustrated by the figures). In the tables this is shown by more than one coloured area in the row or column. When calculating the kappa coefficient the correlated observations (coloured areas) are combined and counted together in the diagonal of the tables, and thereby weighted by a factor of 1,00. See attachment 2 for an illustration of how the cross-tables are combined before the calculation of kappa. Calculation of Cohen's Kappa coefficient (κ) reflects the degree of agreement between the methods compared, taking into the consideration the agreement arisen by chance.

The raw data from the visual and the mechanical readings of CombiScreen 5SYS Plus is shown in attachment 5. The raw data from mechanical readings of the comparison methods is shown in attachment 6.

5.3. CombiScreen 5SYS Plus, visual versus mechanical reading

All readings were carried out in the laboratory at NOKLUS. The lighting conditions were accepted by the manufacturer of the test strip. The urine test strip was compared with the colour codes on the test strip box and the results were read in the order shown on the box. The coloration

of the test pad was read against the colour code on the test strip box that was closest to the colour in the reaction. After finishing the visual reading, a new CombiScreen 5SYS Plus test strip was analysed mechanically at CombiScan 100. The results will be commented on in each section and discussed as a whole in the end of this chapter.

5.3.1. Glucose

The agreement between visual and mechanical reading of glucose with CombiSCreen 5SYS Plus urine test strip is presented in table 1.

Table 1. Visual versus mechanical reading of glucose

CombiScreen, visual	Glucose mmol/L	CombiScreen, mechanical norm	2,8 (1+)	5,6 (2+)	14 (3+)	28 (4+)	56 (5+)	total
	norm	149	0	0	0	0	0	149
	2,8 (1+)	9	7	1	0	0	0	17
	5,6 (2+)	0	6	8	0	0	0	14
	14 (3+)	0	0	4	5	1	0	10
	28 (4+)	0	0	0	2	4	1	7
	≥56 (5+)	0	0	0	1	5	8	14
	total	158	13	13	8	10	9	**211**

Comments

The visual reading of glucose has a different gradation for the answer alternative "5+" (≥56 mmol/L) than the mechanical reading (56 mmol/L). In table 1 there are some more readings lying below than above the diagonal. This indicates that the visual reading is more sensitive to change in colour intensity than the mechanical reading. For glucose 62 samples were registered as positive, the statistical results are therefore more uncertain.

5.3.2. Protein

The agreement between visual and mechanical reading of protein with CombiSCreen 5SYS Plus urine test strip is presented in table 2.

Table 2. Visual versus mechanical reading of protein

CombiScreen, visual	Protein g/L	CombiScreen, mechanical neg	0,3 (1+)	1 (2+)	5 (+)	total
	neg	62	9	0	0	71
	0,15 (trace)	41	26	0	0	67
	0,3 (1+)	6	28	8	0	42
	1 (2+)	0	5	6	0	11
	5 (3+)	0	0	3	7	10
	total	109	68	17	7	**201**

Comments

The visual answer alternative "trace" (0,15 g/L) does not exist for the mechanical reading of protein. The distinction of the green colour shade from "trace" to "1+" is difficult. Room with good lightening is therefore important.

5.3.3. Blood

The agreement between visual and mechanical reading of blood with CombiSCreen 5SYS Plus urine test strip is presented in table 3.

Table 3. Visual versus mechanical reading of blood

CombiScreen, visual	Blood Ery/µL	CombiScreen, mechanical neg	10 (1+)	50 (2+)	300 (3+)	total
	neg	80	3	0	0	83
	5-10 (1+)	17	34	1	0	52
	50 (2+)	0	9	20	13	42
	300 (3+)	0	1	9	14	24
	total	97	47	30	27	**201**

Comments

In table 3 there are some more readings lying below than above the diagonal. This indicates that the visual reading is more sensitive to change in colour intensity than the mechanical reading. There is a disagreement between the visual and the mechanical reading at answer alternative "3+" (300 Ery/µL), where the readings for 23 urine samples disagree and only 14 readings agree.

5.3.4. Leukocytes

The agreement between visual and mechanical reading of leukocytes with CombiSCreen 5SYS Plus urine test strip is presented in table 4.

Table 4. Visual versus mechanical reading of leukocytes

CombiScreen, visual	Leukocytes Leu/µL	CombiScreen, mechanical neg	25 (1+)	75 (2+)	500 (3+)	total
	neg	103	18	5	0	126
	25 (1+)	0	10	26	9	45
	75 (2+)	0	0	1	12	13
	500 (3+)	0	0	0	17	17
	total	103	28	32	38	**201**

Comments

In table 4 all readings are lying in or above the diagonal. Readings lying above the diagonal indicates that the mechanical reading is more sensitive to change in colour intensity than the eye. The test pad for leukocytes gives the visual answer alternatives in different shades of violet dye.

5.3.5. Nitrite

The agreement between visual and mechanical reading of nitrite with CombiSCreen 5SYS Plus urine test strip is presented in table 5.

Table 5. Visual versus mechanical reading of nitrite

CombiScreen, visual	Nitritt µmol/L	CombiScreen, mechanical neg (-)	pos (+)	total
	neg (-)	148	0	148
	pos (+)	6	91	97
	total	154	91	**245**

Comments

The manufacturer states that any degree of pink coloration should be interpreted as a positive nitrite test. Table 5 shows that the eye registers a few more positive nitrite results than the mechanical reading.

5.3.6. Calculation of agreement

The calculated agreement between visual and mechanical reading with CombiScreen 5SYS Plus urine test strip is presented in table 6.

Table 6. Overall agreement and Kappa coefficient

$CombiScreen_{visual}$ vs $CombiScreen_{mechanical}$			
Urine test pad	**Overall agreement (95% confidence interval)**	**Kappa coefficient κ (95% confidence interval)**	**Maximum kappa coefficient (κ_{max})**
Glucose	86% (80 – 90)	0,68 (0,59 – 0,77)*	0,87*
Protein	85% (79 – 89)	0,71 (0,63 – 0,79)*	0,94*
Blood	74% (67 – 80)	0,59 (0,51 – 0,67)*	0,87*
Leukocytes	65% (58 – 72)	0,40 (0,32 – 0,48)*	0,64*
Nitrite	98% (95 – 99)	0,95 (0,91 – 0,99)	0,95

*Calculation based on weighted kappa

Discussion

The CombiScreen Plus package insert states that "as a result of the differing spectral sensitivities of the human eye and the optical system of the instrument, it is not always possible to obtain precise agreement between the values obtained by visual readings and those obtained in the instrument". The calculated agreement between visual and mechanical readings of leukocytes resulted in a kappa coefficient of 0,40. The κ_{max} value for leukocytes verifies that there was an underlying bias between visual and mechanical reading.

For glucose, protein and blood the agreement between visual and mechanical reading was acceptable with $\kappa \geq 0,6$. For nitrite the agreement was good with κ score 0,95.

5.4. CombiScan 100 versus the comparison methods

The accuracy of the new system is assessed by comparing its results with results from two of the market leading products in Norway for analysing of urine samples with test strips; Urisys 1100 and Clinitek Status+. The mechanical readings of the urines were carried out in the following order: CombiScan 100 with the CombiScreen 5SYS Plus test strip, Urisys 1100 with the Combur[5] test and Clinitek Status+ with the Multistix 8 SG test strip. Figure 2 to 5 were made to illustrate that the three urine test strips have unequal answer alternatives and cut-offs. The results will be commented on in each section and discussed as a whole in the end of this chapter.

5.4.1. Glucose

The answer alternatives and cut-offs for the glucose readings at the three different urine analysers are presented in figure 2. The comparison of the mechanical reading of glucose between CombiScan 100 and Urisys 1100 is presented in table 7, and between CombiScan 100 and Clinitek Status+ in table 8.

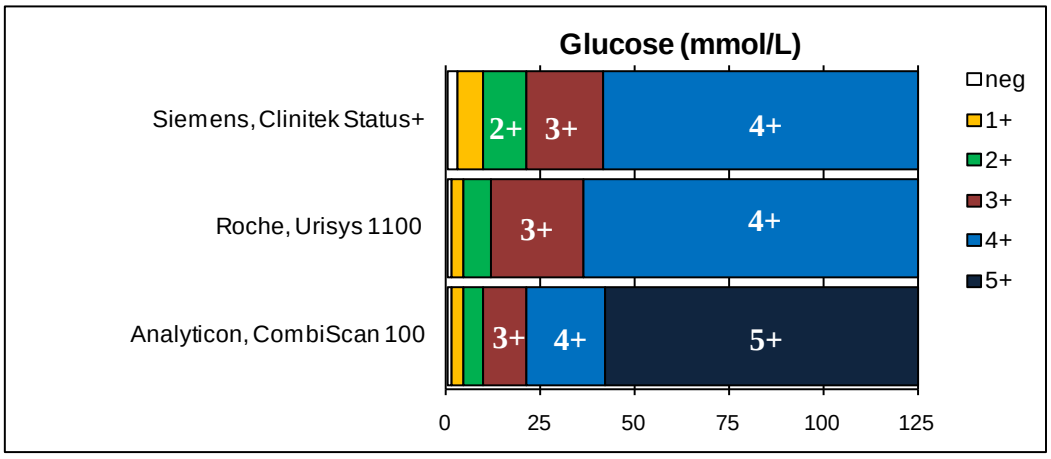

Figure 2. Illustration of transitional points (cut-offs) between the answer alternatives for glucose with the three urine test systems

Table 7. Mechanical reading of glucose, CombiScan 100 versus Urisys 1100

	Glucose	Urisys 1100					
	mmol/L	norm	3 (1+)	6 (2+)	17 (3+)	56 (4+)	**total**
CombiScan 100	norm	141	17	0	0	0	158
	2,8 (1+)	0	1	12	0	0	13
	5,6 (2+)	0	0	11	2	0	13
	14 (3+)	0	0	1	6	1	8
	28 (4+)	0	0	0	3	7	10
	56 (5+)	0	0	0	0	9	9
	total	141	18	24	11	17	**211**

Table 8. Mechanical reading of glucose, CombiScan 100 versus Clinitek Status+

	Glucose	Clinitek Status+					
	mmol/L	neg	5,5 (1+)	14 (2+)	28 (3+)	55/>55 (4+)	**total**
CombiScan 100	norm	158	0	0	0	0	158
	2,8 (1+)	0	13	0	0	0	13
	5,6 (2+)	0	12	1	0	0	13
	14 (3+)	0	1	6	1	0	8
	28 (4+)	0	0	4	5	1	10
	56 (5+)	0	0	0	7	2	9
	total	158	26	11	13	3	**211**

Comments

There was a disagreement in reporting of glucose between CombiScan 100 and Urisys 1100. In table 7 all readings are lying in or above the diagonal. Readings lying above the diagonal indicates that Urisys 1100 is obvious more sensitive to change in colour intensity for glucose than CombiScan 100. Table 8 shows that the agreement in reporting glucose between CombiScan 100 and Clinitek Status+ is good.

5.4.2. Protein

The answer alternatives and cut-offs for the protein readings at the three different urine analysers are presented in figure 3. The comparison of the mechanical reading of protein between CombiScan 100 and Urisys 1100 is presented in table 9, and between CombiScan 100 and Clinitek Status+ in table 10.

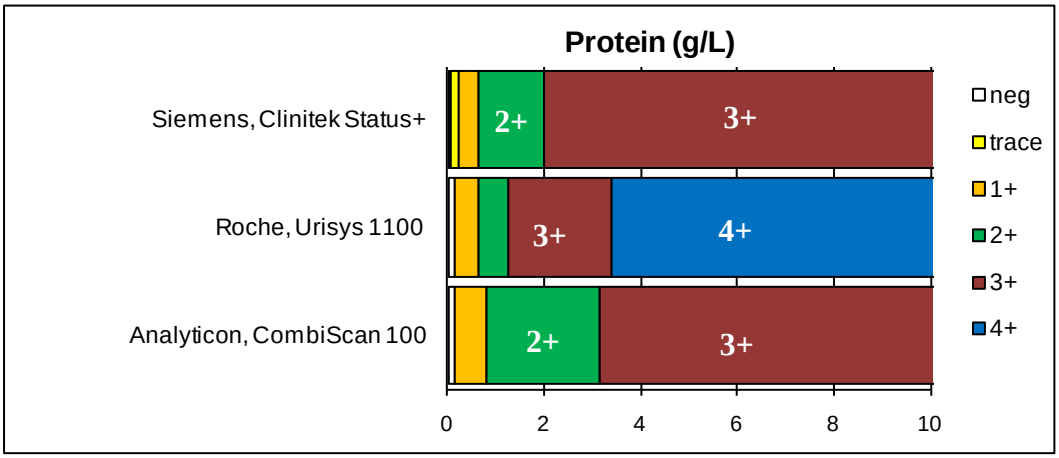

Figure 3. Illustration of transitional points (cut-offs) between the answer alternatives for protein with the three urine test systems

Table 9. Mechanical reading of protein, CombiScan 100 versus Urisys 1100

CombiScan 100	Protein	Urisys 1100					
	g/L	neg	0,25 (1+)	0,75 (2+)	1,5 (3+)	5 (4+)	**total**
	neg	103	6	0	0	0	109
	0,3 (1+)	50	15	3	0	0	68
	1 (2+)	1	6	7	3	0	17
	5 (3+)	0	0	0	7	0	7
	total	154	27	10	10	0	**201**

Table 10. Mechanical reading of protein, CombiScan 100 versus Clinitek Status+

CombiScan 100	Protein	Clinitek Status+					
	g/L	neg	0,15 (trace)	0,3 (1+)	1 (2+)	≥ 3,0 (3+)	**total**
	neg	43	27	34	5	0	109
	0,3 (1+)	1	6	18	40	3	68
	1 (2+)	0	0	0	4	13	17
	5 (3+)	0	0	0	0	7	7
	total	44	33	52	49	23	**201**

Comments

There was a disagreement between CombiScan 100 and Urisys 1100 regarding the answer alternatives “negative” and “1+” (0,3 g/L) for protein. CombiScan read 50 samples as “1+” while Urisys read the same samples as “negative”. The opposite disagreement was seen when CombiScan 100 was compared to Clinitek Status+. Then there was 34 samples registered as “1+” at Clinitek while CombiScan read these samples as “negative”. Clearly, there was a clear discrepancy between the two comparison methods Urisys 1100 and Clinitek Status+, for the component protein.

5.4.3. Blood

The answer alternatives and cut-offs for the erytrocytes readings at the three different urine analysers are presented in figure 4. The comparison of the mechanical reading of erytrocytes between CombiScan 100 and Urisys 1100 is presented in table 11, and between CombiScan 100 and Clinitek Status+ in table 12.

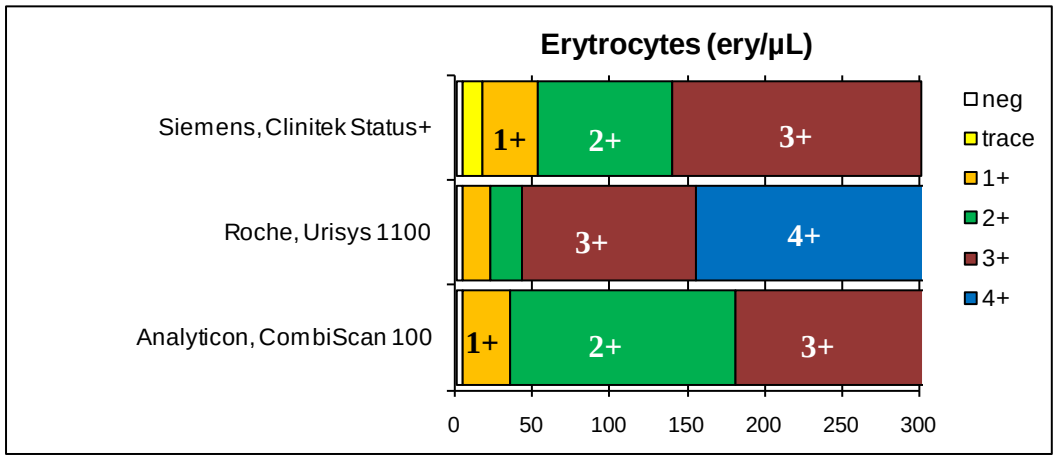

Figure 4. Illustration of transitional points (cut-offs) between the answer alternatives for blood with the three urine test systems

Table 11. Mechanical reading of blood, CombiScan 100 versus Urisys 1100

CombiScan 100	Blood Ery/µL	Urisys 1100 neg	10 (1+)	25 (2+)	50 (3+)	250 (4+)	total
	neg	44	36	17	0	0	97
	10 (1+)	10	7	26	4	0	47
	50 (2+)	0	0	0	15	15	30
	300 (3+)	0	0	0	0	27	27
	total	54	43	43	19	42	**201**

Table 12. Mechanical reading of blood, CombiScan 100 versus Clinitek Status+

CombiScan 100	Blood Ery/µL	Clinitek Status+ neg	10 (trace)	25 (1+)	80 (2+)	200 (3+)	total
	neg	78	19	0	0	0	97
	10 (1+)	7	21	16	3	0	47
	50 (2+)	0	0	5	24	1	30
	300 (3+)	0	0	0	14	13	27
	total	85	40	21	41	14	**201**

Comments

Urisys 1100 gave several more positive test results for blood than CombiScan 100. The producer of the control material (Quantimetrix) states that the negative control may obtain false positive results for blood with Roche analyzers. Roche claims that this will not apply to patient samples. The agreement between CombiScan 100 and Clinitek Status+ was better, but Clinitek was more sensitive to the answer alternative 10 Ery/µL than CombiScan.

5.4.4. Leukocytes

The answer alternatives and cut-offs for the leukocytes readings at the three different urine analysers are presented in figure 5. The comparison of the mechanical reading of leucocytes between CombiScan 100 and Urisys 1100 is presented in table 13, and between CombiScan 100 and Clinitek Status+ in table 14.

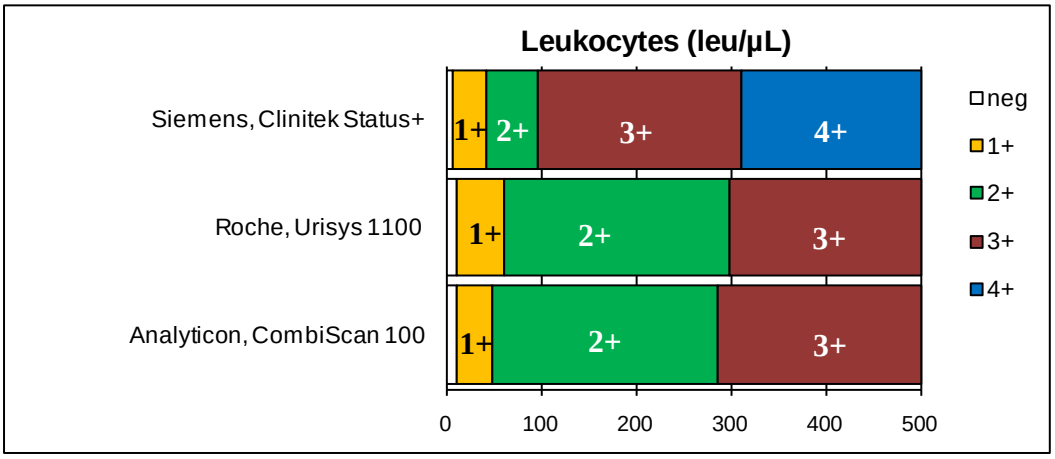

Figure 5. Illustration of transitional points (cut-offs) between the answer alternatives for leukocytes with the three urine test systems

Table 13. Mechanical reading of leukocytes, CombiScan 100 versus Urisys 1100

CombiScan 100 Leukocytes Leu/µL	Urisys 1100 neg	25 (1+)	100 (2+)	500 (3+)	total
neg	61	36	6	0	103
25 (1+)	10	11	6	1	28
75 (2+)	1	4	24	3	32
500 (3+)	0	0	2	36	38
total	72	51	38	40	**201**

Table 14. Mechanical reading of leukocytes, CombiScan 100 versus Clinitek Status+

CombiScan 100 Leukocytes Leu/µL	Clinitek Status+ neg	15 (1+)	70 (2+)	125 (3+)	500 (4+)	total
neg	93	8	2	0	0	103
25 (1+)	3	11	14	0	0	28
75 (2+)	2	4	21	4	1	32
500 (3+)	0	0	4	19	15	38
total	98	23	41	23	16	**201**

Comments

When comparing CombiScan 100 with Urisys 1100 most of the readings for leukocytes lie in or above the coloured areas in table 13. Readings lying above the diagonal indicates that Urisys is more sensitive to change in colour intensity than CombiScan. The agreement in reporting leukocytes between CombiScan 100 and Clinitek Status+ was good.

5.4.5. Nitrite

The comparison of the mechanical reading of nitrite between CombiScan 100 and Urisys 1100 is presented in table 15, and between CombiScan 100 and Clinitek Status+ in table 16.

Table 15. Mechanical reading of nitrite, CombiScan 100 vs. Urisys 1100

CombiScan 100	Nitritt	Urisys 1100		
	µmol/L	neg (-)	pos (+)	**total**
	neg (-)	150	4	154
	pos (+)	4	87	91
	total	154	91	**245**

Table 16. Mechanical reading of nitrite, CombiScan 100 vs. Clinitek Status+

CombiScan 100	Nitritt	Clinitek Status+		
	µmol/L	neg (-)	pos (+)	**total**
	neg (-)	147	7	154
	pos (+)	1	90	91
	total	148	97	**245**

Comments

CombiScan 100 has a different cut-off value for nitrite (0,05 – 0,1 mg/dL) than the two comparison methods (0,05 mg/dL for Urisys 1100 and 0,06 mg/dL for Clinitek Status+). This can explain why some urine samples are registered as positive for nitrite at CombiScan when negative results are shown at the comparison methods. Clinitek Status+ registered a few more positive nitrite results than CombiScan 100.

5.4.6. Calculation of agreement

The calculated agreement between mechanical reading of CombiScan100 and Urisys 1100 are presented in table 17, and between CombiScan 100 and Clinitek Status+ in table 18.

Table 17. Overall agreement and Kappa coefficient

CombiScan$_{mechanical}$ 100 vs Urisys$_{mechanical}$ 1100			
Urine test pad	**Overall agreement (95% confidence interval)**	**Kappa coefficient κ (95% confidence interval)**	**Maximum kappa coefficient (κ_{max})**
Glucose	85% (79 – 89)	0,67 (0,58 – 0,76)*	0,82*
Protein	69% (62 – 75)	0,37 (0,24 – 0,50)*	0,55*
Blood	67% (60 – 73)	0,51 (0,41 – 0,61)*	0,68*
Leukocytes	69% (62 – 75)	0,52 (0,43 – 0,61)*	0,76*
Nitrite	97% (94 – 99)	0,93 (0,88 – 0,98)	1,00

*Calculation based on weighted kappa

Table 18. Overall agreement and Kappa coefficient

CombiScan$_{mechanical}$ 100 vs Clinitek Status+$_{mechanical}$			
Urine test pad	**Overall agreement (95% confidence interval)**	**Kappa coefficient κ (95% confidence interval)**	**Maximum kappa coefficient (κ_{max})**
Glucose	93% (89 – 96)	0,82 (0,75 – 0,90)*	0,93*
Protein	59% (52 – 66)	0,36 (0,26 – 0,45)*	0,62*
Blood	79% (72 – 84)	0,66 (0,58 – 0,75)*	0,80*
Leukocytes	92% (87 – 95)	0,86 (0,80 – 0,92)*	0,97*
Nitrite	97% (94 – 99)	0,93 (0,88 – 0,98)	0,95

*Calculation based on weighted kappa

Discussion

The agreement between CombiScan 100 and Clinitek Status+ for the components glucose, leukocytes and nitrite was good with $\kappa>0,8$. This was verified by a high κ_{max} score. For blood there was an acceptable agreement between the two methods with $\kappa>0,6$.

The agreement between CombiScan 100 and Urisys 1100 was poorer than the agreement between CombiScan 100 and Clinitek Status+. Only the component nitrite showed good agreement with $\kappa>0,8$. Glucose showed an acceptable agreement between the two methods with $\kappa>0,6$. For the components blood and leukocytes the κ_{max} score (0,68 and 0,76 respectively) verifies that there was a discrepancy between CombiScan 100 and Urisys 1100.

Protein was the component that showed the poorest agreement when CombiScan 100 was compared to either of the two comparison methods. The kappa coefficient was <0,40 in both cases. Also a low κ_{max} score (0,55 and 0,62) showed the discrepancy for this component. Table 9 and 10 show that CombiScan 100 gives an overestimation of positive protein readings in proportion to Urisys 1100, and an underestimation in proportion to Clinitek Status+. To find out which of the three methods that lies closest to the true value, the results must be compared to a quantitative method for determination of protein in urine.

A certain deviation between the two comparison methods was observed during the evaluation. This explains a different agreement between CombiScan 100 and the two comparison methods in this evaluation. If two raters disagree, at least one of them must be *incorrect*. If the raters agree, the next step should be to document if they are correct.

5.5. Evaluation of user-friendliness

At the end of the evaluation period, the biomedical laboratory scientist filled in a questionnaire about the user-friendliness of CombiScan 100 with CombiScreen 5SYS Plus test strip.
The questionnaire and expressed opinions are presented in Table 19 to 22. The first column shows what is up for consideration. The second to fourth column show the rating options. The cell with the chosen rating is marked by a coloured frame and bold text. The last row in each table summarises the ratings in the table.

The total rating of each table is not determined by the arithmetic mean of the individual ratings on the rows above. The total ratings are more an overall assessment of the property described on the row or in the headline of the table. A single poor rating can justify an overall poor rating if that 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 19. Assessment of the information in the manual / insert

Information in the manual / insert about:	0 point	1 point	2 point
General impression	Un-satisfactory	Less satisfactory	**Satisfactory**
Table of contents	Un-satisfactory	Less satisfactory	**Satisfactory**
Preparations / Pre-analytic procedures	Un-satisfactory	Less satisfactory	**Satisfactory**
Specimen collection[1]	Un-satisfactory	Less satisfactory	Satisfactory
Measurement / Reading	Un-satisfactory	Less satisfactory	**Satisfactory**
Measurement principle	Un-satisfactory	Less satisfactory	**Satisfactory**
Sources of error	Un-satisfactory	Less satisfactory	**Satisfactory**
Fault-tracing / Troubleshooting	Un-satisfactory	Less satisfactory	**Satisfactory**
Index	**Un-satisfactory***	Less satisfactory	Satisfactory
Readability / Clarity of presentation	Un-satisfactory	Less satisfactory	**Satisfactory**
Available in Danish, Norwegian and Swedish[2]	Un-satisfactory	Less satisfactory	**Satisfactory**
Rating for information in the manual			**Satisfactory**

[1] Not of a question when working with a urine analyzer.
[2]The manual will be translated when the system is launched onto the Scandinavian market.

*Negative comments: There is no index in the manual.

Table 20. Assessment of time factors

Time factors	0 point	1 point	2 point
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 to 30 days	**>30 days**
Rating of time factors			**Satisfactory**

Table 21. Assessment of quality control possibilities

Quality Control	0 point	1 point	2 point
Internal quality control	Un-satisfactory	Less satisfactory	**Satisfactory**
External quality control	Un-satisfactory	Less satisfactory	**Satisfactory**
Stability of quality control material, unopened	<3 months	3 to 5 months	**>5 months**
Stability of quality control material, opened	≤1 days	2 to 6 days	**>6 days or disposable**
Storage conditions of control material, unopened	–20°C	**+2 to +8°C**	+15 to +30°C
Storage conditions of control material, opened	–20°C	**+2 to +8°C**	+15 to +30°C
Usefulness of the Quality Control	Un-satisfactory	Less satisfactory	**Satisfactory**
Rating of quality control			**Satisfactory**

Positive comments: -
Negative comments: -

Table 22. Assessment of the operation facilities

Operation facilities	0 point	1 point	2 point
To prepare the test / instrument	Un-satisfactory	Less satisfactory	**Satisfactory**
To prepare the sample	Un-satisfactory	Less satisfactory	**Satisfactory**
Application of specimen	Un-satisfactory	Less satisfactory	**Satisfactory**
Specimen volume	Un-satisfactory	Less satisfactory	**Satisfactory**
Number of procedure step	Un-satisfactory	Less satisfactory	**Satisfactory**
Instrument / test design	Un-satisfactory	Less satisfactory	**Satisfactory**
Reading / Interpretation of the test result	Un-satisfactory	Less satisfactory	**Satisfactory**
Sources of errors	Un-satisfactory	Less satisfactory	**Satisfactory**
Cleaning / Maintenance	Un-satisfactory	Less satisfactory	**Satisfactory**
Hygiene, when using the test	Un-satisfactory	Less satisfactory	**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	Less satisfactory	**Satisfactory**
Rating of the operation facilities			**Satisfactory**

Comments: The CombiScan urine analyser has the opening of strip holder tray at the right side of the analyser, and not in the front. For inserting the test strip, extra space is therefore required at the laboratory bench.

5.5.1. Assessment of the user-friendliness

The information in the manual or insert was assessed as satisfactory. The biomedical laboratory scientist also thought that the time factors and quality control possibilities, as well as the operating facilities, were satisfactory. The CombiScan 100 system was regarded as user-friendly.

6. References

1. ”European Urinanalysis Guidelines”; T. Kouri, G. Fogazzi, V. Gant, H. Hallander, W. Hofmann. W.G. Guder. Scand J clin Lab Invest – Vol. 60 – Supplement 231, 2000.

2. ”Practical Statistics for Medical Research”; D.G. Altman (403 – 409) 1997.

3. ”Utprøving av analyseinstrumenter”; N.G. Christensen, G. Monsen, S. Sandberg. Alma Mater Forlag, 1997.

4. ”The Kappa Statistic in Reliability Studies: Use, Interpretation, and Sample Size Requirements”; J. Sims, C.C. Wright. Physical Therapy – Vol 85 – no. 3, march 2005.

5. ”Statistical Methods for Rater and Diagnostic Agreement”. http://www.john-uebersax.com/stat/agree.htm

Attachments

1. Facts about the system
2. Cross-tables used in the calculation of Cohen's Kappa coefficient
3. Raw data, internal quality control, CombiScreen 5SYS Plus
4. Raw data, internal quality control, the comparison methods
5. Raw data, results from visual and mechanical readings of CombiScreen 5SYS Plus
6. Raw data, results from mechanical readings of the comparison methods
7. "SKUP-info". Norwegian summary for primary healthcare
8. List of evaluations organised by SKUP
9. Comments from the manufacturer

Attachments with raw data are included only in the report to Medinor and Analyticon.

Facts about the analyser

a) Name of the analyser	***CombiScreen 5SYS Plus and CombiScan 100***

Physical dimensions	*width: 26,5 cm* *depth: 13,5 cm* *height: 9 cm*
Manufacturer (with address)	*Analyticon Biotechnologies AG* *Am Muehlenberg 10* *35104 Lichtenfels / Germany* *www.analyticon-diagnostics.com*
Distributor (with address)	*Denmark* *Medinor A/S* *Park Alle 350E, st* *2605 Brøndby, Danmark* *info@medinor.dk*
	Norway *Medinor AS* *Nils Hansens vei 4* *Postboks 94 Bryn* *N-0611 Oslo* *www.medinor.no*
	Sweden *Medinor AB* *Box 1215 | 181 24 Lidingö* *Sverige* *kundservice@medinor.com*

b) Analysis menu, sample materials and volume of the analysis

Component	Sample materials	Volume of the analysis
urine test strip, *evaluation visually or by analyzer*	*urine*	*about 10 ml of urine (reagent tube)*

c) Analysis principles (reference to the instruction manual)

Parameter	Principle
Glucose	*Detection of glucose in the urine is based on the glucose oxidase-peroxidase-chromogen reaction (green colour reaction)*
Protein	*Sensitivity for albumin. This test is based on the "protein error" principle of the indicator that changes colour from yellow to green.*
Blood	*Detecting occult blood in urine. This test is based on the peroxidative activity of haemoglobin and myoglobin (green colour reaction)*
Nitrites	*This test is based on the Griess reaction (pink colour reaction)*
Leucocytes	*This test is based on the activity of esterase from granulocytes (violet colour reaction)*

d) Area of analysis

Component	Area of analysis	Designation
urine test strip, evaluation visually or by analyzer	*routine urine diagnostics*	*For use as a preliminary screening test for diabetes, liver diseases, haemolytic diseases, urogenital and kidney disorders and metabolic abnormalities.*

e) Time for analysis per component (precisely stated)

Component	Pre-analysis time (with an explanation)	Analysis time
All parameters, evaluation by analyzer	*urine sample must be brought to room temperature*	*dipping, incubation, analyzer measurement + printout: 1,5 minutes*
Glucose visual evaluation	*urine sample must be brought to room temperature*	*dipping, incubation, visual evaluation: 1 minute*
Protein visual evaluation	*urine sample must be brought to room temperature*	*dipping, incubation, visual evaluation: 1 minute*
Blood visual evaluation	*urine sample must be brought to room temperature*	*dipping, incubation, visual evaluation: 1 minutes*
Nitrites visual evaluation	*urine sample must be brought to room temperature*	*dipping, incubation, visual evaluation: 1 minutes*
Leucocyte visual evaluation	*urine sample must be brought to room temperature*	*dipping, incubation, visual evaluation: 1-2 minutes*

f) Calibration

Is calibration possible?	*not necessary*
How often is calibration recommended?	*not applicable*
Number of standards	*not applicable*
Who should carry out calibration?	*not applicable*

g) Recommended maintenance

Maintenance	How often?
Clean strip holder with lint-free tissue	*after each measurement*
Clean strip holder with disinfectant and rinsing water, be sure it is dry before removing it to the analyzer	*daily*

h) Control materials

Is control material available (from the producer or other companies?	*a) strip holder with fixed grey strip to test the performance of the optical unit of the analyzer* *b) 2-level control solution set (CombiScreenControl PN) to test the system analyzer + test strip*

a) Name of the analyser	***CombiScreen 5SYS Plus and CombiScan 100***

i) Marketing

In which country is the analyser marketed?	*Globally*
When did the analyser first appear on the Scandinavian market?	*not yet launched in Scandinavia*
When did the analyser receive CE approval?	*2004*

j) Language

In which Scandinavian language is the manual?	*Danish. Norwegian. Swedish, Finnish* *(to be translated)*

k) Memory

What is the storage capacity of the analyser and what is stored?	*460 results in total:* *460 patient results, or* *400 patient results + 30 qc-results (2 level)* *(if the lockout mode is activated)*
Is it possible to identify patients?	*Yes*
If yes, describe this:	*patient ID can be entered* *a)by external barcode reader* *b) by external keyboard* *The patient ID appears on the printout*

l) Power supply

Electric network connection	*Yes*
Battery	*No*
If yes, which type and how many batteries	*not applicable*

m) Electronic communication

Can a printer be connected to the analyser?	*Not necessary, instrument has got an internal printer*
Can a barcode reader be connected to the analyser?	*Yes*
Interface	*Yes*
If yes, which port is required?	*USB*
Communication method	*unidirectional and bidirectional*
Transfer mode	*Serial transfer*
Transfer protocol	*Other protocol (Serial line interface protocol description available)*

n) Standards and controls

	Standard	Control
Name	Not applicable	*CombiScreen Control PN (2 level set)*
Volume	Not applicable	*2 x 15 ml*
Shelf life unopened	Not applicable	*storage 2-8°C, until printed expiry*
Shelf life opened	Not applicable	*storage 2-8°C, 3 months or 20 dipstick immersions*
Any comments:	Not applicable	-

o) Reagents

Component	Time and temperature, unopened	Time and temperature, opened
urine test strip (up to 11 parameters)	*2 – 30 °C until printed expiry*	*2 – 30 °C until printed expiry*
Any comments:	**-**	**-**

p) Additional information

-

Raw data, internal quality control CombiScreen Control Normal and Pathological

Date	Glucose	Protein	Blood	Nitrite	Leukocytes	Lot no.	Comments
24.nov	norm	neg	neg	neg	neg	a	
26.nov	norm	neg	neg	neg	neg	a	
27.nov	norm	neg	neg	neg	neg	b	
30.nov	norm	neg	neg	neg	neg	b	
01.des	norm	neg	neg	neg	neg	b	
02.des	norm	neg	neg	neg	neg	b	
08.des	norm	neg	neg	neg	neg	b and c	
09.des	norm	neg	neg	neg	neg	c	
10.des	norm	neg	neg	neg	neg	c	
11.des	norm	neg	neg	neg	neg	c	
14.des	norm	neg	neg	neg	neg	a	
15.des	norm	neg	neg	neg	neg	a	New bottle
16.des	norm	neg	neg	neg	neg	a	
17.des	norm	neg	neg	neg	neg	b	
18.des	norm	neg	neg	neg	neg	c	
21.des	norm	neg	neg	neg	neg	c	
05.jan	norm	neg	neg	neg	neg	c	New bottle
07.jan	norm	neg	neg	neg	neg	b	
08.jan	norm	neg	neg	neg	neg	c	
13.jan	norm	neg	neg	neg	neg	b	
14.jan	norm	neg	neg	neg	neg	c	
18.jan	norm	neg	neg	neg	neg	c	
19.jan	norm	neg	neg	neg	neg	b	
01.feb	norm	neg	neg	neg	neg	c	
08.feb	norm	neg	neg	neg	neg	a	
09.feb	norm	neg	neg	neg	neg	b	
23.feb	norm	neg	neg	neg	neg	a	
24.feb	norm	neg	neg	neg	neg	a	

Date	Glucose	Protein	Blood	Nitrite	Leukocytes	Lot no.	Comments
24.nov	28	1	50	pos	500	a	
26.nov	28	1	50	pos	500	a	
27.nov	28	1	50	pos	500	b	
30.nov	28	1	50	pos	500	b	
01.des	14	1	50	pos	500	b	
02.des	28	1	50	pos	500	b	
08.des	28	1	50	pos	500	b and c	
09.des	28	1	50	pos	500	c	
10.des	28	1	50	pos	500	c	
11.des	28	1	50	pos	500	c	
14.des	28	1	50	pos	500	a	
15.des	28	1	50	pos	500	a	New bottle
16.des	56	1	50	pos	500	a	
17.des	28	1	50	pos	500	b	
18.des	28	1	50	pos	500	c	
21.des	28	1	50	pos	500	c	
05.jan	14	1	50	pos	500	c	New bottle
07.jan	28	1	50	pos	500	b	
08.jan	28	1	50	pos	500	c	
13.jan	28	1	50	pos	500	b	
14.jan	28	1	50	pos	500	c	
18.jan	28	1	50	pos	500	c	
19.jan	28	1	50	pos	500	b	
01.feb	28	1	50	pos	500	c	
08.feb	28	1	50	pos	500	a	
09.feb	28	1	50	pos	500	b	
23.feb	28	1	50	pos	500	a	
24.feb	28	1	50	pos	500	a	

Raw data, internal quality control, the comparison method Urisys 1100 (Roche).

Quantimetrix the Dipper, Urine dipstick control 1 & 2.

Date	Glucose	Leukocytes	Nitrite	Protein	Blood*	Lot no. Strip	Comments
24.nov	norm	neg	neg	neg	10	23052245	
26.nov	norm	neg	neg	neg	10	23052245	
27.nov	norm	neg	neg	neg	neg	23052245	
30.nov	norm	neg	neg	neg	neg	23052245	
01.des	norm	neg	neg	neg	10	23052245	
02.des	norm	neg	neg	neg	10	23052245	
08.des	norm	neg	neg	neg	neg	23052245	
09.des	norm	neg	neg	neg	10	23052245	
10.des	norm	neg	neg	neg	10	23052245	New bottle
11.des	norm	neg	neg	neg	neg	23052245	
14.des	norm	neg	neg	neg	neg	23052245	
15.des	norm	neg	neg	neg	neg	23052245	
16.des	norm	neg	neg	neg	neg	23052245	
17.des	norm	neg	neg	neg	neg	23052245	
18.des	norm	neg	neg	neg	neg	23052245	
21.des	norm	neg	neg	neg	neg	23052245	
05.jan	norm	neg	neg	neg	neg	23052245	New bottle
07.jan	norm	neg	neg	neg	10	23052245	
08.jan	norm	neg	neg	neg	neg	23052245	
13.jan	norm	neg	neg	neg	10	23052245	
14.jan	norm	neg	neg	neg	neg	23052245	
18.jan	norm	neg	neg	neg	neg	23052245	
19.jan	norm	neg	neg	neg	neg	23052245	New bottle
01.feb	norm	neg	neg	neg	neg	23052245	
08.feb	norm	neg	neg	neg	neg	23052245	
09.feb	norm	neg	neg	neg	neg	23052245	
23.feb	norm	neg	neg	neg	neg	23052245	
24.feb	norm	neg	neg	neg	neg	23052245	

*The producer of the control material states that some customers may obtain false positive results for blood.

Date	Glucose	Leukocytes	Nitrite	Protein	Blood	Lot no. strip	Comments
24.nov	56	500	pos	0,75	250	23052245	
26.nov	56	500	pos	0,75	250	23052245	
27.nov	56	500	pos	0,75	250	23052245	
30.nov	56	500	pos	0,75	250	23052245	
01.des	56	500	pos	0,75	250	23052245	
02.des	56	500	pos	0,75	250	23052245	
08.des	56	500	pos	0,75	50	23052245	
09.des	56	500	pos	0,75	50	23052245	
10.des	56	500	pos	0,75	250	23052245	New bottle
11.des	56	500	pos	0,75	250	23052245	
14.des	56	500	pos	0,75	250	23052245	
15.des	56	500	pos	0,75	250	23052245	
16.des	56	500	pos	0,75	250	23052245	
17.des	56	500	pos	0,75	250	23052245	
18.des	56	500	pos	0,75	250	23052245	
21.des	56	500	pos	0,75	50	23052245	
05.jan	56	500	pos	0,75	250	23052245	New bottle
07.jan	56	500	pos	0,75	250	23052245	
08.jan	56	500	pos	0,75	250	23052245	
13.jan	56	500	pos	0,75	250	23052245	
14.jan	56	500	pos	0,75	250	23052245	
18.jan	56	500	pos	0,75	50	23052245	
19.jan	56	500	pos	0,75	250	23052245	New bottle
01.feb	56	500	pos	0,75	250	23052245	
08.feb	56	500	pos	0,75	250	23052245	
09.feb	56	500	pos	0,75	50	23052245	
23.feb	56	500	pos	0,75	25	23052245	
24.feb	56	500	pos	0,75	250	23052245	New bottle

Raw data, internal quality control, the comparison method Clinitek Status+ (Siemens).

Chek-Stix Combo Pak Control +/- .

Date	Glucose	Blood	Protein	Nitrite	Leukocytes	Lot no. strip	Comments
24.nov	neg	neg	neg	neg	neg	9G25C	
26.nov	neg	neg	neg	neg	neg	9G25C	
27.nov	neg	neg	neg	neg	neg	9G25C	
30.nov	neg	neg	neg	neg	neg	9G25C	
01.des	neg	neg	neg	neg	neg	9G25C	
02.des	neg	neg	neg	neg	neg	9G25C	
08.des	neg	neg	neg	neg	neg	9G25C	
09.des	neg	neg	neg	neg	neg	9G25C	
10.des	neg	neg	neg	neg	neg	9G25C	
11.des	neg	neg	neg	neg	neg	9G25C	
14.des	neg	neg	neg	neg	neg	9G25C	
15.des	neg	neg	neg	neg	neg	9G25C	
16.des	neg	neg	neg	neg	neg	9G25C	
17.des	neg	neg	neg	neg	neg	9G25C	
18.des	neg	neg	neg	neg	neg	9G25C	
21.des	neg	neg	neg	neg	neg	9G25C	
05.jan	neg	neg	neg	neg	neg	9G25C	
07.jan	neg	neg	neg	neg	neg	9G25C	
08.jan	neg	neg	neg	neg	neg	9G25C	
13.jan	neg	neg	neg	neg	neg	9G25C	
14.jan	neg	neg	neg	neg	neg	9G25C	
18.jan	neg	neg	neg	neg	neg	9G25C	
19.jan	neg	neg	neg	neg	neg	9G25C	
01.feb	neg	neg	neg	neg	neg	9G25C	
08.feb	neg	neg	neg	neg	neg	9J11DC	New lot
24.feb	neg	neg	neg	neg	neg	9J11DC	

Date	Glucose	Blood	Protein	Nitrite	Leukocytes	Lot no. strip	Comments
24.nov	5,5	200	1,0	pos	70	9G25C	
26.nov	14,0	200	1,0	pos	70	9G25C	
27.nov	5,5	200	1,0	pos	70	9G25C	
30.nov	5,5	200	1,0	pos	70	9G25C	
01.des	5,5	200	1,0	pos	70	9G25C	
02.des	5,5	200	1,0	pos	125	9G25C	
08.des	5,5	200	1,0	pos	125	9G25C	
09.des	5,5	200	1,0	pos	125	9G25C	
10.des	5,5	200	1,0	pos	125	9G25C	
11.des	5,5	200	1,0	pos	70	9G25C	
14.des	5,5	200	1,0	pos	70	9G25C	
15.des	5,5	200	1,0	pos	70	9G25C	
16.des	5,5	200	1,0	pos	70	9G25C	
17.des	5,5	200	1,0	pos	70	9G25C	
18.des	5,5	200	1,0	pos	70	9G25C	
21.des	5,5	200	1,0	pos	70	9G25C	
05.jan	5,5	200	1,0	pos	70	9G25C	
07.jan	5,5	200	1,0	pos	70	9G25C	
08.jan	5,5	200	1,0	pos	70	9G25C	
13.jan	5,5	200	1,0	pos	70	9G25C	
14.jan	5,5	200	1,0	pos	70	9G25C	
18.jan	5,5	200	1,0	pos	70	9G25C	
19.jan	5,5	200	1,0	pos	125	9G25C	
01.feb	5,5	200	1,0	pos	70	9G25C	
08.feb	5,5	200	1,0	pos	70	9J11DC	New lot
24.feb	5,5	200	1,0	pos	70	9J11DC	

SKUP-info

CombiScreen 5SYS Plus urinstrimmel og CombiScan 100 urinstrimmel avleser fra Analyticon Biotechnologies AG

Sammendrag fra en utprøving i regi av SKUP

Konklusjon
Visuell mot maskinell avlesning av CombiScreen 5SYS Plus: **Godt samsvar for nitritt og akseptabelt[1] samsvar for glukose, protein og blod. Ikke tilfredsstillende samsvar mht leukocytter.**
Sammenligning med Clinitek Status+: **Godt samsvar for glukose, leukocytter og nitritt. Akseptabelt samsvar for blod. Ikke tilfredsstillende samsvar mht protein.**
Sammenligning med Urisys 1100: **Godt samsvar for nitritt og akseptabelt samsvar for glukose. Ikke tilfredsstillende samsvar mht blod, leukocytter og protein.**
Utprøvingen gir ikke svar på hvilken av de tre metodene som ligger nærmest sann verdi.

CombiScreen 5SYS Plus urinstrimmel og CombiScan 100 avleser er produsert av Analyticon Biotechnologies AG og forhandles i Skandinavia av Medinor. Urinstrimmelen har testfelt for glukose, protein, blod, nitritt og leukocytter.

Utprøvingen ble utført under optimale betingelser av laboratorieutdannet personale. Det ble samlet inn ca. 300 urinprøver fra pasienter på sykehus og i primærhelsetjenesten. Avlesning av CombiScreen 5SYS Plus på CombiScan 100 ble sammenlignet med urinstrimmelen Combur[5] Test avlest på Urisys 1100 (Roche) og urinstrimmelen Multistix 8 SG avlest på Clinitek Status+ (Siemens). Visuell og maskinell avlesning av CombiScreen 5SYS Plus ble også sammenlignet.

Resultater
Det var godt samsvar mellom visuell og maskinell avlesning av CombiScreen 5SYS Plus for nitritt og akseptabelt samsvar for glukose, protein og blod. For leukocytter var det ikke tilfredsstillende samsvar mellom de to avlesningsmåtene.
Det var godt samsvar mellom CombiScan 100 og Clinitek Status+ for glukose, leukocytter og nitritt, og akseptabelt samsvar for blod.
Samsvaret mellom CombiScan 100 og Urisys 1100 var godt for nitritt og akseptabel for glukose.
Det var ikke tilfredsstillende samsvar mellom CombiScan 100 og Urisys 1100 for avlesning av blod og leukocytter.
Når det gjelder protein var det uenighet mellom de tre avlesningsmetodene. CombiScan 100 gir flere positive avlesninger av protein enn Urisys 1100 og færre positive avlesninger enn Clinitek Status+.
Denne utprøvingen gir ikke svar på hvilken av de tre metodene som ligger nærmest sann verdi.

Brukervennlighet
Bioingeniøren vurderte CombiScan-systemet til å være brukervennlig.

Tilleggsinformasjon
En fullstendig rapport fra utprøvingen av CombiScreen 5SYS Plus og CombiScan 100, SKUP/2010/79*, finnes på SKUPs nettside, www.skup.nu. Opplysninger om pris fås ved å kontakte leverandør. Laboratoriekonsulentene i NOKLUS kan gi nyttige råd om analysering av urinstrimmel på legekontor. De kan også orientere om det som finnes av alternative metoder/utstyr.

[1] Samsvaret i kategorien ”Akseptabel” er verken god eller dårlig.

List of previous SKUP evaluations

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

SKUP evaluations from number 51 and further

Evaluation no.	Component	Instrument/testkit	Producer
SKUP/2010/79*	Urine test strip	CombiScreen 5SYS Plus and CombiScan 100	Analyticon Biotechnologies AG
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/2008/69*	Strep A	Diaquick Strep A test	Dialab GmbH
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

*A report code followed by an asterisk, indicates that the evaluation for instance is a pre-marketing evaluation, and thereby confidential. A pre-marketing evaluation can result in a decision by the supplier not to launch the instrument onto the Scandinavian marked. If so, the evaluation remains confidential. The asterisk can also mark 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 market any more.

SKUP evaluations from number 1 — 50

Evaluation no.	Component	Instrument/test kit	Producer
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 & Johnson
SKUP/2005/39	Glucose[1]	OneTouch Ultra	LifeScan, Johnson & Johnson
SKUP/2004/38*	Glucose	GlucoSure Plus	Apex Biotechnology Corp.
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	QuickVue u-hCG	Quidel Corporation
SKUP/2004/34*	u-hCG	RapidVue u-hCG	Quidel Corporation
SKUP/2004/33	PT (INR)	Hemochron Jr. Signature	ITC International Technidyne Corp
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

For comments regarding the evaluations, please see the indications on the first page.

NOKLUS / SKUP
Box 6165
5892 Bergen

NORWAY

27. May 2010

SKUP-report 2010/79 „Combi Screen 5SYS Plus and Combi Scan 100“ urinalysis system

Dear ladies and gentlemen,

We wish to offer our sincere thanks for performing such a well-designed evaluation study on the Combi Screen 5SYS Plus urine test strips and the Combi Scan 100 urine analyzer. We would like to use this opportunity to comment on two major findings from our view:

1. User friendliness
The system was evaluated as user-friendly, which is the highest possible score. This agrees very well to the feedback that we get from our customers.

2. Agreement to comparison methods
The evaluation was performed against two systems manufactured by the market leaders in urinalysis, which are both globally well established. During the study, there was a certain deviation observed between these systems. The overall agreement between these comparison methods is in the same range as the agreement of the Analyticon system to the comparison methods each. The deviation between the market leading systems demonstrates the commonly accepted deviation in urinalysis according to our experience and hence the equal performance of the Analyticon system to the comparison methods.

We were very pleased to participate in this highly reputable independent study, and we really appreciate the hard work that was invested in this study and the very professional communication with the members of SKUP.

Yours sincerely,

Solvi Haga
Product Manager
Medinor ASA

Dr. Klaus Langer
Director Business Development
Analyticon Biotechnologies AG

Dr. Sonja Lauterbach
Product Management
Analyticon Biotechnologies AG