Point-of-Care testing
*Principles and Practicals*

Hannele Kangas  
*PhD, Docent*
LABORATORY MEDICINE AND MOLECULAR DIAGNOSTICS 2013  
27.3.2013

HUSLAB laboratories

Primary health care center laboratories > 50  
Centralized hospital laboratories >10
The Role of Primary Healthcare Laboratory Services

- Taking blood samples in primary healthcare center laboratories
  - Venipunctures >1,2 million/ year
- ECG, Spirometry, gynecological screening
- **Point-of-Care testing in laboratories (CRP, Hb, Glucose, urine tests etc.)**
  - POCT tests : > 33 000 CRP tests/year
- Point-of-Care Concept for our customers (in co-operation with Division of Clinical Chemistry and Hematology)
- Education and guidelines in preanalytics (e.g. blood, urine sampling)

Primary Healthcare Laboratory Services as Numbers

- Ca 200 km wide, 60 km long
- Employees > 350
- Labs and other offices > 50
- Venipunctures > 1 000 000 / year
Point-of-care testing, POCT

- ISO 22870:2006:
  Testing that is performed near or at the site of a patient with the result leading to possible change in the care of the patient

Point-of-care testing in HUSLAB - various users

- Primary Health Care Center laboratories
- Hospital laboratories
  - (only in a few laboratories)
- Customers
  - Hospital departments (e.g. blood gases)
  - Primary Health care centers (CRP, HbA1c, INR, Hb, urine test, TnT)
  - Nurses (INR)
There has to be medical need for performing POCT!

What does that mean?

**POCT is a test that has an immediate influence in patient care, treatment decisions, medication or to some other closely patient related activity.**

Test result has to be accurate

→ Quality has to be controlled!
→ Trained staff that is motivated to POCT!

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**When to use POC-tests**

• Evaluation of the need of the POC test
  – Clinical need
    • The purpose of the test e.g. diagnosis, treatment, screening
  – The need for faster turn around time
    • HUSLAB laboratories are spread over a wide area, transportation to core laboratory
  – Patient convenience (e.g. saving time, smaller sample volume)
  – Costs
The most rapidly growing sector in clinical chemistry
- How to ensure quality?

HUSLAB’s POC organization

CEO

Division of Clinical Chemistry and Hematology

Expert Doctors and Chemists

Tecnicians

Hospitals/ Special Healthcare

Ward-POC  Policlinic-POC  Laboratory-POC

Division of Primary Healthcare Laboratory Services

POC-Chemist  Clinical Chemist, quality

POC-Technician

Primary Health Care Centers

Health center lab POC  Health Center POC  Health Visitor POC  Ward POC
Recommendations and standards

Quality guidelines

- Labquality Expert Group, 2009: National guidance for the use of POC testing by health care services
- Standards SFS 22870, SFS 15189
- CLSI POCT4-A2

Quality control of POC-tests

1. Clinical need for the test
2. Selection of a POC-device
3. Planning of validation or verification in association with the experts
4. Validation/verification of the POC-test
5. Quality control
   - Internal quality assessment
   - External quality assessment
6. Examination of the quality results
7. Acceptance of the results
   - Results accepted
   - Results not accepted
8. Implementation of the POC device for routine use, training of the personnel

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HUSLAB offers customers (in primary healthcare and special healthcare) comprehensive POC services.
- POC devices and reagents
- Quality management
- Support
- Instructions and training
- POC-IT in future?
- CRP, Hb, urine analysis (basic screening), HbA1c, INR, TnT, WBC, blood gas analytics

POC Concept for customers

Selection of POC devices

- POC devices should fulfill the essential criteria of the IVD-directive 2007/47/EC including validation by the manufacturer

- The CE marking of IVD devices is not adequate and sufficient evidence that the POCT device really is fit and acceptable for the intended use
POC devices

- Harmonized equipment
  - Each laboratory has similar POCT devices, also customers, out-laboratories
- Electrical inspection
- Validation
  - Pre-validation before purchase
  - Validation of new type of device
  - Verification of other individual devices

POC Concept

- CRP
- Hb
- Urine analytics (basic screening)
- HbA1c
- INR
- TnT
- WBC
- Blood gas analytics
POC Devices

- HUSLAB owns the devices and delivers them to the customers
- HUSLAB puts devices out to tender
  - Harmonized equipment
    - Laboratories
    - Customers, out-laboratories
  - Performance (CV, Bias...)
  - Usability

→ Testing before decision

Method validation

- ISO /IEC 17025:2005 cl.5.4.5.1
  Validation is the confirmation by examination and the provision of objective evidence that the particular requirements for a specific intended use are fulfilled
Method validation

• Confirms, that the specific test is suitable for its intended use

• Results can be used to confirm the quality and reliability of the test

Method validation

• All medical devices including POC-testing devices, need to be validated or verified before they are taken into routine use
  – Whenever the conditions change for which the method has been validated (e.g. samples with different matrix)
  – Whenever the method or application is changed
Method verification

- Verification of a chemical test confirms the accuracy of the results and that the test is suitable for its specified use

- Done for each POCT test in HUSLAB

Validation protocol of POC tests at HUSLAB

- Labquality Expert Group, 2009: National guidance for the use of POC testing by health care services
- HUSLAB has a POC-center which coordinates the validations and verifications of new POC-devices
  - Similar POC devices in the laboratory and outside laboratory
- Validation plan
  - Group of experts carefully designs the validation plan for each validation
- All new POC test devices are either validated or verified before they are accepted for use
Validation protocol of POC tests at HUSLAB

• Each POC device method of a certain analyzer type is validated; reference method is the corresponding core lab method

• Verification is done for consecutive POC test devices which have been previously validated

• The usability of the POC device is tested
  – Easy to use, noise level, points of misusages

Validation parameters

- Trueness
- Robustness
- Linearity and range
- Limit of quantification
- Limit of detection
- Specificity
- Precision
- Accuracy
Validation parameters Accuracy: Trueness + Precision

- Method comparison in validation: POC test results are compared against those obtained with the corresponding laboratory method (~50-100 samples)

- HUSLAB has goals for bias for analyzers and POC devices

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**Good correlation, good quality - or is it?**

Device A: $R^2 = 0.99$ ($y=1.002x-0.04$)  
Device B: $R^2 = 0.99$ ($y=1.036x-1.12$)
Validation parameters
Method comparison

• Two different calibration and reagent lots are used during the validation, if possible

• If the sample material is not suitable for both methods (e.g. capillary blood, whole blood, plasma or serum) two consecutive samples are drawn from the patient (by permission) and used in validation

Validation parameters: Precision

• Within-assay repeatability
  – Two different control sample levels or min 30 patient samples analyzed twice

• Between-day repeatability
  – Two different control sample levels (20 samples)

• Reproducibility (precision between laboratories, CVlab)
Validation parameters: Precision

- Precision of a POC test might not be as good as achieved through automated lab analyzer → the increased imprecision should be weighed against the clinical advantages of using a POC test device

CRP-POCT

What is the indication for testing CRP with POCT?

Advantages?

- For infection diagnostics
  - Test result is needed immediately for treatment plan (discharge, discharge with antibiotics, hospital)
- Shorter TAT
  - Cost efficient
  - Patient friendly
Validation parameters

Analytical variation

- As with all laboratory tests, analytical variation of POC tests should preferably be based on biological variation.

<table>
<thead>
<tr>
<th></th>
<th>HUSLAB CV %</th>
<th>CV % POC-device</th>
</tr>
</thead>
<tbody>
<tr>
<td>CRP</td>
<td>7.3 %</td>
<td>14%</td>
</tr>
<tr>
<td>HbA1c</td>
<td>3.2 %</td>
<td>3.6%</td>
</tr>
</tbody>
</table>

- Desirable analytical variation is half of the intra-individual variation.

Small-scale verification of a previously validated new POC test device in HUSLAB

<table>
<thead>
<tr>
<th>Validation</th>
<th>Verification</th>
</tr>
</thead>
<tbody>
<tr>
<td>Method comparison for a laboratory method</td>
<td>50 – 100 samples</td>
</tr>
<tr>
<td>Repeatability, Within-assay Between day</td>
<td>20-30</td>
</tr>
<tr>
<td></td>
<td>20</td>
</tr>
</tbody>
</table>

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### POC devices

**Amount in HUSLAB**

<table>
<thead>
<tr>
<th>Device, analytics</th>
<th>Amount Laboratories</th>
<th>Amount Out-laboratories</th>
</tr>
</thead>
<tbody>
<tr>
<td>Afinion, CRP</td>
<td>60</td>
<td>60</td>
</tr>
<tr>
<td>Afinion, HbA1c</td>
<td>3</td>
<td>40</td>
</tr>
<tr>
<td>HemoCue, Hb</td>
<td>32</td>
<td>41</td>
</tr>
<tr>
<td>Clinitek Status, urine screening</td>
<td>30</td>
<td>20</td>
</tr>
<tr>
<td>CoaguChek, INR</td>
<td>1</td>
<td>46</td>
</tr>
<tr>
<td>Glucose</td>
<td>60</td>
<td></td>
</tr>
</tbody>
</table>
Quality management of the POC-devices

- The result of the POC-test has to be as reliable as the test done in the central laboratory, because it has immediate effects to the care of the patient
  - Test should not be repeated
  - The functionality of the test has to be confirmed continuously (controls)
  - The personnel using the POC-devices has to know how to do the quality control and how to interpretate the quality results
  - The personnel has to know the preanalytical errors concerning the POC-device, sample collection, handling etc.
POC-process in laboratory
- potential sources of errors in every step!

Pre-analytical phase
- (Request)
- (Patient Instructions)
- Identification of the patient
- Taking the sample
- Identification of the sample
- Handling, storage, transport
- Labeling the sample
- Validity of the sample

Analytical phase
- Taking the sample
- Doing the POC-test
- Quality management

Post-analytical phase
- Acceptance of the result
- Answering the result
- POC-IT, laboratory information system, patient records
- Interpreting the result, decision of treatment
- Quality management:
  - External quality management, comparison of the level of results to the central laboratory result level

POC personnel in Primary Healthcare Laboratory Services

- Clinical Chemist, point-of-care
- Clinical Chemist, quality
- Technician, point-of-care
- Technicians, POC contact persons in the different areas (60)
Motivated, trained personnel

- Training of the personnel
  - Each person using POC-tests is trained for the usage of the tests
  - Documented training
  - The foundation of the quality management!

Internal Quality assessment

- When opening a new reagent pack
- If the POCT device is not used for over a week
- If the POCT device has given an error-message
- After every service (~once a month)
- Whenever there is a suspicion that something is wrong with the reagent cassettes, cuvettes, POCT device etc.)
External quality assessment

• Participation to the Labquality external quality assessment services 2-4 times / year
• Laboratory technician specialized in POCT analyses the results. If there are abnormalities in the results, she consults the chemist
• Out-laboratories: the staff analyses the samples; laboratory interpretes the results and informs the out-laboratories staff

Support

• Supporting technicians (contact persons) are nominated to all customers
  – Helps in daily problems

• Chemists, POC-technician and all other experts available
  – Contact form supplied
Instructions and education

• Instructions
  – Also POCT-devices need distinct instructions for use
  – Forms for quality control if the results do not go directly to the laboratory information system or POC-IT is not in use
  – All instructions supplies for custumers

• Education for HUSLAB POC-personnel
  – Training organized by HUSLABs POC-center (1-2 times/year)
  – Training outside HUSLAB

Training Concept: New Customer

• All personnel will be trained by HUSLAB
  – Instructions
  – How to use devices
  – Quality assessment
  – Sampling

• Information session
• Lecture and Hands-On training
  – As many times as needed

• On-Site Startup support 1-2 days, if needed
• Refresh training when needed
• Feedback gathering
Traceability of the POC result

- The POC result has to be traceable
- **The identification of the patient and the transfer of the result to the correct patient—the most important step in the process**
  - Who took the sample?
  - Who did the test?
  - How is the result documented?
- The POC-test has to be documented so that it is clearly separated from the other tests done in the laboratory

Follow up

- Continuous follow-up for the use of the POC-devices
  - Is there still clinical need for the use of the tests?
  - Costs
  - Quality
  - Education of the personnel
- Are there new more suitable POC-devices on the market?
POC-IT

• Data management system for POC-devices
  Device is connected to IT-system and further to LIS and HIS

• Helps to control expanding amount of POC-devices

• Enables traceability of patient and control results

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POC-IT

• Enables and helps
  – Quality management
    • Controls can be checked using remote control
    • If the satisfactory quality is not achieved, device can be withdrawn from the system
  – User competence follow-up

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Advantages in POCT

• When performed correctly POCT will speed up the process in patient care

• Cost efficiency
  - Costs for the whole process: Costs per test, Instrument expenses, staff resources vs. savings when patient treatment is speeded up
  - Increased patient satisfaction

• No sample transportation and storage related risks

• Small sample volume
POCT related risks

- Preanalytical errors
- Errors when analyzing the sample
- Quality controls are not used
- Analytical quality of the POC method is not sufficient
- Amount of waste
- Costs
  - POCT usually more expensive than lab tests in general
  - Unnecessary use of the instrument
- Traceability problems
- In self testing
  - Errors in understanding results
  - Instructions are not understood
  - Patient does not receive training on how to use the instrument

Point-of-Care testing

Principles and Practicals
1. Indentification of the patient

2. Warm the hands
   - under the warm water, rub the hands
   - dry well (prevents drop from spreading)

3. Finger prick
   - middle or ring finger, from the side, lancet 2,3 mm

4. Hold finger firmly
   - prick deep enough, high quality sample is taken without unnecessary squeezing (Interstitial fluid!)

5. Wipe drop/s off
   - Final drop has to be big enough
Practicals I

- Afinion AS100 (Axis-Shield) Point-of-Care instrument
- CRP measuring range 5 – 200 mg/l
- Capillary blood (1,5 ul)
Figure 1.1 The main components of the Afion™ CRP Test Cartridge.

Table 1.1 Description of the Afion™ CRP Test Cartridge components and reagents. The numbers in the left column refer to the numbers in Figure 1.1 above.

<table>
<thead>
<tr>
<th>Component</th>
<th>Function/Component</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Dosing device</td>
<td>For collection of patient sample or control.</td>
</tr>
<tr>
<td>a Closed position</td>
<td></td>
</tr>
<tr>
<td>b First position</td>
<td></td>
</tr>
<tr>
<td>2 Capillary</td>
<td>1.5 mL glass capcity to be filled with sample matrix.</td>
</tr>
<tr>
<td>a Capillary paper</td>
<td></td>
</tr>
<tr>
<td>b Membrane tube</td>
<td>Plastic terminated paper.</td>
</tr>
<tr>
<td>c Conjugate solution</td>
<td>Anti-CRP antibodies labelled with ultra-small gold particles.</td>
</tr>
<tr>
<td>d Wash solution</td>
<td>Phosphate buffered sodium chloride and detergents.</td>
</tr>
<tr>
<td>e Shutoff fluid</td>
<td>Blocker for buffer and detergents.</td>
</tr>
<tr>
<td>3 Handle</td>
<td>For correct finger grip.</td>
</tr>
<tr>
<td>4 Reproare label</td>
<td>Contains assay and lot specific information for the Analyst.</td>
</tr>
<tr>
<td>5 Optical reading area</td>
<td>Area for absorption measurement.</td>
</tr>
<tr>
<td>7 ID area</td>
<td>Space for written or labeled sample identification.</td>
</tr>
</tbody>
</table>
The Afinion analysis principle

• A Test Cartridge with patient sample or control is placed in the cartridge chamber of the Afinion™ AS100 Analyzer.
• By closing the lid, the Test Cartridge is transported into the analysis compartment of the Analyzer.
• Test and lot specific information is obtained from the barcode label, which then initiates the processing of the Test Cartridge.
• The sample and reagents are automatically transferred between the wells.

The chemical principle of the Afinion CRP test

• Test Cartridge contains all the reagents necessary for measuring the CRP concentration
• The sample is automatically diluted with a liquid that also lyses the blood cells.
• If the sample is whole blood, the hematocrit value is estimated from transmission measurement of the hemoglobin.
• The sample mixture is sucked through the membrane coated with anti-CRP antibodies, and all CRP in the sample is concentrated onto this membrane.
• The conjugate solution containing anti-CRP antibodies labeled with ultra-small gold particles is then sucked through the membrane.
• The gold-antibody conjugate binds to the immobilized CRP on the membrane, which will turn red-brown.
• Excess gold-antibody conjugate is removed by a washing solution. The Afinion™ AS100 Analyzer measures the colour intensity of the membrane, and this is proportional to the amount of CRP in the sample.
Method

- A monochrome solid-state camera monitors the entire process.
- When the assay is completed, light-emitting diodes (LEDs) illuminate the final reaction area, which can be either a coloured membrane or a reaction well.
- The camera detects the reflected or transmitted light, which is converted to a test result and displayed on the touch screen.

Axis-Shield PoC AS
Oslo, Norway
Hb measurement

General
The HemoCue Hb 201+ is a system used for the determination of the total amount of hemoglobin in whole blood. The system consists of a specially designed analyzer with specially designed microcuvettes containing dried reagents. The microcuvette serves as pipette, reaction vessel and as a measuring microcuvette. No dilution is required. The hemoglobin measurement takes place in the analyzer, which follows the progress of the reaction until the steady state has been reached. The system is factory-calibrated against the hemoglobincyanide (HCN) method, the international reference method for the determination of the hemoglobin concentration in blood.
Hb measurement

HemoCue Hb 201

**Principle:** Sodium deoxycholate hemolyses the erythrocytes and hemoglobin is released. Sodium nitrite converts hemoglobin to methemoglobin which, together with sodium azide, becomes azidenethemoglobin. The absorbance is measured at two wavelengths (570 nm and 880 nm) in order to compensate for turbidity in the sample.

**Measuring time:** Results within 15–60 seconds

**Sample material:** Capillary or venous blood

**Sample volume:** 10 µL

**Quality control:** Built-in self test

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1. To perform a test using capillary blood, the cuvette holder should be in its loading position. The display will show three flashing dashes and the HemoCue symbol.
2. Make sure the patient’s hand is warm and relaxed. Use only the middle or ring finger for sampling. Avoid fingers with rings on.
3. Clean the finger with alcohol or a suitable disinfectant and allow to dry or wipe off with a dry, lint-free wipe.
4. Using your thumb, lightly press the finger from the top of the knuckle towards the tip. This stimulates the blood flow towards the sampling point.
5. For best blood flow and least pain, sample at the side of the fingertip, not in the center.
6. While applying light pressure towards the fingertip, puncture the finger using a lancet.
7. Wipe away the first 2 or 3 drops of blood.
8. Re-apply light pressure towards the fingertip until another drop of blood appears.

9. When the blood drop is large enough, fill the microcuvette in one continuous process. Do NOT refill.
10. Wipe off excess blood from the outside of the microcuvette with a clean, lint-free wipe, being careful not to touch the open end of the microcuvette, which could result in blood being drawn out of the microcuvette.
11. Look for air bubbles in the filled microcuvette. If present, discard the microcuvette and fill a new microcuvette from a new drop of blood. Small bubbles around the edge can be ignored.
Thank you for your attention!