External Quality Control

Piet Meijer
Outline:

• Introduction
• Laboratory Process
• External Quality Control
• External Quality Control Survey
• Evaluation Quality Controls Results
• Use of Quality Control Results
Introduction
Dr. Marie Chantal Nzayisaba meets with a Congolese patient at the health center in Maratane refugee camp in Mozambique

Laboratory testing and diagnosis

- Qualitative
- Semi-quantitative
- Quantitative

Correct Test Result?
HOW TO ASSURE THE CORRECTNESS OF A LABORATORY RESULT?
Laboratory Test Process
Total Testing Process

Physician

External Quality Control

Physician

Laboratory
Laboratory Test

Test Result

- Environment
- Sample
- Personnel
- Consumables
- Equipment
- Calibrator
- Reagents
- Analytical principle
Figure 4. Fishbone Diagram for Identification of Potential Failure Modes

External Quality Control

CLSI EP23-A
CORRECT TEST RESULT

Each test result is affected by both imprecision and inaccuracy

External Quality Control

Internal Quality Control

PRECISION

ACCURACY
Accuracy is the difference between the measured test result and the “true” test result. Accuracy is also known as systematic error or bias.
Accuracy

- Qualitative
  - Do you observe the correct blood cell abnormality?

- Semi-quantitative
  - Do you observe the correct colour change?

- Quantitative
  - Do you measure the correct titer or concentration?
Is the test result correct, yes or no?
How can I know the test result is correct?
Control of Analytical Process

IQC

Does the analytical test system provides reliable result?

EQC

Does the analytical test system provides accurate result?

External Quality Control
<table>
<thead>
<tr>
<th>IQC</th>
<th>EQC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Are my results reliable?</td>
<td>Are my results accurate?</td>
</tr>
<tr>
<td>• Within-run precision</td>
<td>• Deviation from “true” value</td>
</tr>
<tr>
<td>• Within-day precision</td>
<td>• Between-laboratory variation</td>
</tr>
<tr>
<td>• Between-run precision</td>
<td>• Within-laboratory performance</td>
</tr>
<tr>
<td>• Between-day precision</td>
<td>• Method performance</td>
</tr>
<tr>
<td></td>
<td>• Equipment performance</td>
</tr>
</tbody>
</table>

IQC ≠ EQC
External Quality Control
External Quality Control

Inter-laboratory comparison of test results of unknown samples with a focus on participant and method performance evaluation, including the trueness of measurement, with the meaning to support quality improvement according to the needs of the laboratory.
External Quality Control

- Measure of deviation
- Measure of laboratory quality
- Benchmarking tool
- Warning-system for problems
- Monitor of changes in technology and testing practices
- Prevention of mistakes
- Improvement in testing performance

QUALITY ASSURANCE AND IMPROVEMENT
External Quality Control

Unknown patient sample → Correct test result

Unknown control sample → Accurate test result
EQC Process

EQC Organiser → Distribution samples → Participant

Evaluation of results → Report

Test of samples → Return of results

Participant

Troubleshooting and/or improvement → Evaluation of report
External Quality Control is always organised by an independent organisation to guarantee that the laboratory receive unknown samples. The organiser is responsible for the design and the execution of the External Quality Control Programme.
A laboratory that participate in an external quality control programme organised by an independent organisation.
Distribution and Receipt of samples

- Sample selection
- Preparation of survey
- Distribution of samples
- Receipt of samples
- Storage of samples
EQA samples should be treated as regular patient plasmas and included in the normal daily analytical process in the laboratory. The regularly used methods should be applied. No special treatment of the samples is allowed. Results should be reported similar as a result of a patient is reported.
HAEMATOLOGY MORPHOLOGY PROFICIENCY TESTING SCHEME
2017/2018

TRIAL: 0417

BLOOD SMEAR: CLINICAL INFORMATION

SLIDE A
A 43 year old female known with metastatic breast cancer presented to casualty with weakness and fatigue. Her Hb was 4.7g/dl and she was transfused and referred to oncology.

The full blood count and platelets shows the following:

<p>| | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>White Cell Count</td>
<td>16.46</td>
<td>10^9/l</td>
</tr>
<tr>
<td>Red Cell Count</td>
<td>2.89</td>
<td>10^12/l</td>
</tr>
<tr>
<td>Haemoglobin</td>
<td>8.8</td>
<td>g/dl</td>
</tr>
<tr>
<td>Haematocrit</td>
<td>0.275</td>
<td>l/l</td>
</tr>
<tr>
<td>Mean Cell Volume</td>
<td>95</td>
<td>fl</td>
</tr>
<tr>
<td>Mean Cell Haemoglobin</td>
<td>30.5</td>
<td>pg</td>
</tr>
<tr>
<td>Mean Cell Haemoglobin Conc.</td>
<td>32.2</td>
<td>g/dl</td>
</tr>
<tr>
<td>Red Cell Distribution Width</td>
<td>22.4</td>
<td>%</td>
</tr>
<tr>
<td>Platelets</td>
<td>28</td>
<td>10^9/l</td>
</tr>
<tr>
<td>Mean Platelet Volume</td>
<td>12.0</td>
<td>fl</td>
</tr>
</tbody>
</table>

Required: Differential white cell count, white cell morphology, red cell morphology, platelet morphology, interpretative comment, diagnosis/differential diagnosis and suggest further investigations.
SURVEY INSTRUCTIONS MAIN PROGRAMME

<table>
<thead>
<tr>
<th>SURVEY</th>
<th>2019-M1</th>
</tr>
</thead>
<tbody>
<tr>
<td>WEBSITE OPEN</td>
<td>5 March 2019</td>
</tr>
<tr>
<td>Closing date result submission</td>
<td>2 April 2019</td>
</tr>
<tr>
<td>Expected report issue date</td>
<td>30 April 2019</td>
</tr>
<tr>
<td>Result submission via</td>
<td><a href="http://www.ecat.nl">www.ecat.nl</a> (after login)</td>
</tr>
<tr>
<td>For questions or assistance</td>
<td><a href="mailto:info@ecat.nl">info@ecat.nl</a></td>
</tr>
</tbody>
</table>

STORAGE AND STABILITY
Unreconstituted lyophilised plasma should be stored at 2-8°C. Reconstituted plasma should preferably be used within 1 hour after reconstitution. Plasma should be kept at room temperature after reconstitution. For immunological methods the reconstituted plasma can be stored for 1 month at −20°C.

RECONSTITUTION
For proper reconstitution the vial must reach room temperature before adding the water. Dissolve the contents of each vial in sterile, distilled, room temperature water. For the exact volume of water to be used: see table reverse side. Leave the vial for 5 minutes. Swirl the vial gently to mix and leave for a further 15 minutes for complete reconstitution. Before use mix the vial again gently.
See for more information the complete list with samples on the reverse side.
### Samples Survey 2019-M1:

<table>
<thead>
<tr>
<th>Sample code</th>
<th>Volume (mL)</th>
<th>Vials per sample code</th>
<th>Module Code on vial</th>
<th>Module</th>
</tr>
</thead>
<tbody>
<tr>
<td>19.33</td>
<td>1.00 (per vial)</td>
<td>2</td>
<td>Thrombophilia - I</td>
<td>Thrombophilia - I; Antithrombin (activity and antigen), Protein C (activity [chromogenic and clotting] and antigen), Protein S activity, Protein S antigen (total and free)</td>
</tr>
<tr>
<td>19.34</td>
<td>1.00 (per vial)</td>
<td>2</td>
<td>Thrombophilia - I</td>
<td>Thrombophilia - I (see above)</td>
</tr>
<tr>
<td>19.35</td>
<td>1.00</td>
<td>1</td>
<td>Thrombophilia - II</td>
<td>Thrombophilia - II; for APC Resistance only</td>
</tr>
<tr>
<td>19.36</td>
<td>1.00</td>
<td>1</td>
<td>Thrombophilia - II</td>
<td>Thrombophilia - II; for APC Resistance only</td>
</tr>
<tr>
<td>19.37</td>
<td>0.75 (per vial)</td>
<td>2</td>
<td>Lupus</td>
<td>Lupus Anticoagulant</td>
</tr>
<tr>
<td>19.38</td>
<td>1.00 (per vial)</td>
<td>2</td>
<td>CFM - I</td>
<td>Coagulation Factors - I (Factor VIII, IX, XI and XII)</td>
</tr>
<tr>
<td>19.39</td>
<td>0.75 (per vial)</td>
<td>2</td>
<td>CFM - I</td>
<td>Coagulation Factors - I (Factor VIII, IX, XI and XII)</td>
</tr>
<tr>
<td>19.40</td>
<td>0.75 (per vial)</td>
<td>2</td>
<td>CFM - II</td>
<td>Coagulation Factors - II (Factor II, V, VII and X)</td>
</tr>
<tr>
<td>19.41</td>
<td>1.00 (per vial)</td>
<td>2</td>
<td>CFM - II</td>
<td>Coagulation Factors - II (Factor II, V, VII and X)</td>
</tr>
</tbody>
</table>
The participant returned the results to the EQAC organiser. The organiser evaluate the results. Depending on the type of programme (qualitative, semi-quantitative or quantitative) specific statistical procedures are used.
**RESULTS OF ANTITHROMBIN ACTIVITY**

**USE SAMPLE**: 96.01  
**EXERCISE**: 96/01  
**LAB. CODE NO.**: 

<table>
<thead>
<tr>
<th>Kit:</th>
<th>Name + Type</th>
<th>Producer</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>CHROMOGENX</td>
</tr>
</tbody>
</table>

If none, specify reagents and suppliers:

S 2238  
Thrombin  
(Comtec - modified)

**Type of method:** CHROMOGENIC ASSAY

**Automation:** YES / NO  
If YES, specify machine: ACL 5000 Plus

**Your (normal) Reference Range:** 0.82 - 4.8

**Antithrombin result for Sample 96.01:** 0.56  
**Units:** IU

---

**Antithrombin activity**

**Antithrombin antigen (%)**

**Antithrombin antigen (mg/dL)**
Return of results

Be aware that results are correct and complete reported to the EQC organiser, included requested details on method, equipment etc. Incomplete or wrong reporting may affect your individual performance evaluation

► 75 – 85% of errors in the evaluation are related to transcriptional errors by the participant.

Example: Fibrinogen
sample 1: 2.4 g/L
sample 2: 38 g/L
Evaluation of results

- Qualitative
  - Ordering of qualitative results

- Semi-quantitative
  - Ordering of semi-quantitative results

- Quantitative
  - Statistical evaluation of quantitative results
Qualitative results

Positive

Negative

√

X
Semi-Quantitative results

Tabela 2.2 Análise de concordância

<table>
<thead>
<tr>
<th>Resultados do lab. participante</th>
<th>Resultados esperado</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Negativo</td>
</tr>
<tr>
<td>Negativo</td>
<td>Correcto</td>
</tr>
<tr>
<td>1-9 bacilos/100 campos</td>
<td>Correcto</td>
</tr>
<tr>
<td>1+</td>
<td>BFP</td>
</tr>
<tr>
<td>2+</td>
<td>AFP</td>
</tr>
<tr>
<td>3+</td>
<td>AFP</td>
</tr>
<tr>
<td>Correcto</td>
<td>Sem erro (10 pontos)</td>
</tr>
<tr>
<td>EQ = Erro de Quantificação</td>
<td>Erro menor (5 pontos)</td>
</tr>
<tr>
<td>BFN = Baixo Falso Negativo</td>
<td>Erro menor (5 pontos)</td>
</tr>
</tbody>
</table>

External Quality Control
Semi-Quantitative results
### Overview of the combinations of activator and lysis agents used

<table>
<thead>
<tr>
<th>Lysis Agent</th>
<th>Human Trombin</th>
<th>Bovine Trombin</th>
<th>Calcium Chloride</th>
<th>Agkistrodon rhodastoma venom</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acetic Acid</td>
<td>3</td>
<td>8</td>
<td>6</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Chloro Acetic Acid</td>
<td>0</td>
<td>0</td>
<td>21</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Urea</td>
<td>6</td>
<td>9</td>
<td>51</td>
<td>0</td>
<td>4</td>
</tr>
<tr>
<td>Other</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

### Results

- Abnormal (FXIII < 1%) 23
- Normal (FXIII > 1%) 3

Your Result 1: Abnormal (FXIII < 1%)  
Your Result 2:  
Your Result 3:  

---

External Quality Control
Quantitative results

Principle of the evaluation of quantitative results is the comparison of the result of the participant with the target value or assigned value.

Example:

Difference between target and result participant
Quantitative results

Key factor for the evaluation of quantitative EQC results is the assessment of the assigned value or target value.

Possibilities

1. Assessment on the basis of participant results
2. Assessment on the basis of a reference method procedure
3. Assessment on the basis of expert laboratories
Quantitative results

Assessment of the assigned value or target value on the basis of participant results.

Procedure

1. Collect all results and harmonise results if different units are used.
2. Exclude aberrent outlying results
3. Calculate mean/median and standard deviation using robust statistics (minimum effect of outliers)
   Alternatively: Use a procedure to exclude outliers and then calculate mean/median
Performance evaluation

Kind of performance evaluations in EQA:

• Individual participants performance
• assay-principle performance
• method performance
• instrument performance
• commercial vs home-made reagents performance
• calibration performance
• lot-to-lot performance
Performance evaluation

Individual performance indicator:

A numerical indicator representing the position of the individual lab result with respect to the consensus value – measure for accuracy
Z-score:

Z-score = Standard Deviation Index

*It describes the systematic error or bias of the individual result from the consensus value as a multiplier of the standard deviation.*

\[
Z\text{-score} = \frac{\text{lab result} - \text{target}}{\text{sd}}
\]
Performance evaluation

-2 \leq Z\text{-score} \leq 2
Satisfactory
   No signal

-3 \leq Z\text{-score} < -2
   Questionable
   Warning signal

2 < Z\text{-score} \leq 3

Z\text{-score} < -3
Unsatisfactory
   Action signal

External Quality Control

AMERICAN SOCIETY FOR MICROBIOLOGY

CCQL-PLP EDUCATION
Target: 100 mmol/L
SD: 5 mmol/L
Lab result: 92 mmol/L

Z-score = (92 – 100) / 5 = -1.60
# NHLS Haematology Proficiency Testing Scheme

## Final Report

**Contact:** Laboratorv Manager  
**Laboratory:** MAPUTO  
**Region:** EXT004

**Trial Number:** 117  
**Cell Counter:** SYSMEX XE 2100  
**Coag Instrument:** CA 500  
**Lab Code:** 1482  
**Date of Report:** 16 May 2017

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Results</th>
<th>Out of Limits</th>
<th>z-score</th>
<th>No</th>
<th>Method Mean</th>
<th>SD</th>
<th>CV (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>WCC sample W</td>
<td>4.71</td>
<td></td>
<td>-0.83</td>
<td>264</td>
<td>4.85</td>
<td>0.17</td>
<td>3.5</td>
</tr>
<tr>
<td>WCC sample X</td>
<td>11.14</td>
<td></td>
<td>-0.80</td>
<td>263</td>
<td>11.43</td>
<td>0.36</td>
<td>3.1</td>
</tr>
<tr>
<td>RCC sample W</td>
<td>3.44</td>
<td></td>
<td>-0.58</td>
<td>271</td>
<td>3.47</td>
<td>0.06</td>
<td>1.7</td>
</tr>
<tr>
<td>RCC sample X</td>
<td>3.36</td>
<td></td>
<td>-0.77</td>
<td>268</td>
<td>3.40</td>
<td>0.05</td>
<td>1.6</td>
</tr>
<tr>
<td>Hb sample W</td>
<td>10.7</td>
<td></td>
<td>-0.64</td>
<td>262</td>
<td>10.79</td>
<td>0.14</td>
<td>1.3</td>
</tr>
<tr>
<td>Hb sample X</td>
<td>9.2</td>
<td></td>
<td>-1.18</td>
<td>265</td>
<td>9.35</td>
<td>0.12</td>
<td>1.3</td>
</tr>
<tr>
<td>HCT sample W</td>
<td>0.298</td>
<td></td>
<td>-0.67</td>
<td>267</td>
<td>0.306</td>
<td>0.012</td>
<td>3.8</td>
</tr>
<tr>
<td>HCT sample X</td>
<td>0.257</td>
<td></td>
<td>-0.88</td>
<td>268</td>
<td>0.265</td>
<td>0.009</td>
<td>3.3</td>
</tr>
<tr>
<td>MCV sample W</td>
<td>86.6</td>
<td></td>
<td>-0.50</td>
<td>263</td>
<td>88.1</td>
<td>3.02</td>
<td>3.4</td>
</tr>
<tr>
<td>MCV sample X</td>
<td>76.5</td>
<td></td>
<td>-0.56</td>
<td>260</td>
<td>77.9</td>
<td>2.50</td>
<td>3.2</td>
</tr>
</tbody>
</table>
Performance evaluation

Cumulative z-score

WCCW  WCCX  RCCW  RCCX  HBW  HBX  HCTW  HCTX  MCVW  MCVX  PLTW  PLTX  ESR  INR1  INR2
### Interpretação de resultado final

<table>
<thead>
<tr>
<th>Analise Estatística</th>
<th>Amostra QC90</th>
<th></th>
<th>Amostra QC91</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CD4 %</td>
<td>CD4 #</td>
<td>CD4 %</td>
<td>CD4 #</td>
</tr>
<tr>
<td>Reportado pelo laboratório</td>
<td>13.41</td>
<td>143</td>
<td>36.55</td>
<td>456</td>
</tr>
<tr>
<td>Média do grupo</td>
<td>16.1</td>
<td>143.2</td>
<td>37.1</td>
<td>370.7</td>
</tr>
<tr>
<td>Residual</td>
<td>-2.7</td>
<td>-11.0</td>
<td>-0.6</td>
<td>85.3</td>
</tr>
<tr>
<td>Desvio padrão</td>
<td>1.1</td>
<td>32.6</td>
<td>1.16</td>
<td>60.59</td>
</tr>
<tr>
<td>Índice de desvio padrão</td>
<td>-2.52</td>
<td>-0.3</td>
<td>-0.51</td>
<td>1.4</td>
</tr>
</tbody>
</table>
Performance evaluation

Position individual lab

Assay principles

Whole distribution
Performance evaluation
MINISTÉRIO DA SAÚDE
INSTITUTO NACIONAL DE SAÚDE

PROGRAMA NACIONAL DE AVALIAÇÃO EXTERNA DE QUALIDADE
Ensaio 37

<table>
<thead>
<tr>
<th>Data de Recepção</th>
<th>Data limite de reporte</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fevereiro/2018</td>
<td>Fevereiro/2018</td>
</tr>
</tbody>
</table>

Data de Análise: Fevereiro/Maio-2018
Retorno dentro do Prazo: Sim

PAINEL DE PROFICIÊNCIA
Avaliação Externa de Qualidade de CD4 – Imunologia Celular

Relatório Individual (Final)

Código do Participante: [Redacted]
Troubleshooting

Troubleshooting and/or improvement

Evaluation of report

Receipt report

Evaluation report

Corrective actions

Implementation

Documentation Storage

External Quality Control
Figure 4. Fishbone Diagram for Identification of Potential Failure Modes

1. Samples
   - Sample Integrity
     - Lipemia
     - Hemolysis
     - Interfering substances
     - Clotting
     - Incorrect tube
   - Sample Presentation
     - Bubbles
     - Inadequate volume

2. Operator
   - Operator Capacity
     - Training
     - Competency
   - Operator staffing
     - Short staffing
     - Correct staffing

3. Reagents
   - Reagent Degradation
     - Shipping
     - Storage
     - Used past expiration
     - Preparation
   - Quality Control Material Degradation
     - Shipping
     - Storage
     - Used past expiration
     - Preparation

4. Laboratory Environment
   - Atmospheric Environment
     - Dust
     - Temperature
     - Humidity
   - Utility Environment
     - Electrical
     - Water quality
     - Pressure

5. Measuring System
   - Calibrator Degradation
     - Shipping
     - Storage
     - Used past expiration
     - Preparation
   - Instrument Failure
     - Software failure
     - Optica drift
     - Electronic instability
   - Inadequate Instrument Maintenance
     - Dirty optics
     - Contamination
     - Scratches

Incorrect Test Result
EQC and the patient

Monitoring Effect → Treatment → Diagnosis

LABORATORY TEST RESULTS

Correct test result: Yes or No?
EQC and the patient

- Qualitative
  - Semi-quantitative
  - Quantitative

With an incorrect test result there is a risk for misdiagnosis of a patient or wrong monitoring of treatment.
Quality assurance is an important tool in the delivery of reliable laboratory results to the physician.