How to Achieve Harmonisation of Laboratory Testing
- The Complete Picture

Sverre Sandberg,
Noklus / EFLM
The need for harmonization
The possibility for harmonization

- Two examples
An EQAS for Porphyrias

In the same scheme:
- Pre-analytical
- Analytical
- Post-analytical

EQAS for porphyrias
36 specialist laboratories

Samples from one patient are circulated within 48 hours.

Case history

What analysis would have been performed

Analytical results

How was the report form

What diagnosis

Conclusions

Large variation in what tests that were requested with a certain diagnostic problem

Large analytical variation with CV\text{inter} ab 40-60\%. (No reference method, no harmonization)

Large variation in report forms and the commenting

Diagnostic Conclusion

25 out of 36 participating laboratories would have made the correct diagnosis of Acute intermittent porphyria.

Five laboratories stated that some form of acute porphyria was a possible diagnosis, but would have asked for a new sample.

Six laboratories ruled out porphyria or gave no suggestion for a diagnosis.

Primary care
Traveling HIV Tester and Counselor in Kenya.
Service providers come by bicycle to remote areas with poor roads. In isolated desert regions, service delivery by camel is being developed.  

How to achieve harmonisation of laboratory testing — The complete picture

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Harmonisation of Laboratory Testing

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The Clinical and Laboratory Standards Institute refers to a definition of ‘(method) harmonization’ as ‘the process of recognizing, understanding, and explaining differences while taking steps to achieve uniformity of results, or at a minimum, a means of conversion of results such that different groups can use the data obtained from assays interchangeably’.¹

In the following series of articles in Part A of this two-part series on the Harmonisation of Laboratory Testing, the scope of harmonisation addressed is more far-reaching than method harmonisation, and includes other aspects of pathology testing namely:

1. Standardisation of pathology units and terminology.
2. Harmonisation of report formats where there are patient safety issues, e.g. left to right versus right to left reporting.
3. Harmonised reference intervals (RIs) and decision limits.

The Electronic Health Record (EHR) and patient safety issues are driving the need for harmonised methodology, terminology and units of reporting in pathology. Analytical tests use different methods that may not have been ‘harmonised’ or which may have different units of reporting. Those who analytical’ phase (‘Right test at the Right time for the Right patient’) to the analytical aspects and reporting of critical tests, through to consumer education and the meaning of laboratory tests in lay terms (‘post-post-analytical’ phase).

It is important to identify where harmonisation is potentially beneficial across all pathology disciplines and to involve the relevant stakeholders (Table). Both the pathology laboratory community and clinicians using the tests need to become involved in the harmonisation process.

In the following papers several of the key issues that have important implications for pathology harmonisation are reviewed and discussed.

Mario Plebani, who leads the International Federation of Clinical Chemistry and Laboratory Medicine Working Group on Laboratory Errors and Patient Safety (IFCC WGLIEPS), describes the quality indicators (QIs) to detect pre-analytical errors in laboratory testing. The 16 QIs developed for the pre-analytical phase include those from outside the control of the laboratory, e.g. test requesting, patient and sample identification and sample collection (so-called ‘pre-pre-analytical phase’ QIs), to QIs that cover all steps of the laboratory ‘pre-analytical phase’, e.g. sample preparation and storage. Through an understanding of the risks to patients undergoing laboratory testing, standardised operating
Anamnesis Clinical Findings

Pre-pre (test requesting)

Pre-analytical phase

Analysing

Post-analytical (report)

Diagnosis Treatment Monitoring

Post-post (interpretation)
Harmonization

Successful harmonisation of all the different phases and steps depends both on the availability of evidence-based knowledge as well as systems that can initiate, monitor and maintain the results of the harmonisation.

Some steps of the TTP can be harmonised internationally, while others will best be harmonised locally or nationally. There are several parties that can be drivers and stakeholders in this process.
A challenge for the laboratory is especially the harmonization of the extra-analytical phases

Gaps, breaches in continuity of care which lead to errors, are often detected at the interface of more than one area of responsibility or professional role, which emphasizes the need for attention to all aspects of patient testing.

- and although we theoretically know what to do – are we able to do it?

Between the idea and the reality
(Between the motion and the act)
Falls the shadow

Thomas S. Elliot
Most important with this lecture is to generate a discussion.

I will give suggestions as to what level of harmonization is possible, who could be responsible for initiating, facilitating and monitoring the effects of harmonisation, and what barriers that might exist.
Table 1
The likely achievable levels of harmonisation are shown for the different phases and steps of the total testing process where the laboratory profession can have a significant impact. The potential for harmonisation will vary with different laboratory tests and the prevalence of the associated diseases. Successful harmonisation in the likely achievable level will furthermore depend on the ability of organisations and stakeholders to cooperate and on healthcare systems being advanced enough to incorporate the required changes. In many cases the listed barriers can be turned into drivers/facilitators and vice versa.

<table>
<thead>
<tr>
<th>The total testing process</th>
<th>Harmonisation</th>
<th>Likely achievable level</th>
<th>Drivers/facilitators</th>
<th>Barriers</th>
<th>Structures for monitoring</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phase</td>
<td>Steps</td>
<td>Responsible</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre- and pre-analytical</td>
<td>Test requesting</td>
<td>Clinician with the involvement of laboratory specialist</td>
<td>International procedure on how to achieve harmonisation of test ordering</td>
<td>International and national clinical and laboratory societies/organisations</td>
<td>Strong (clinical) opinion leaders</td>
</tr>
<tr>
<td>Procedures related to laboratory testing (eg. test requesting, sample drawing at the GP's office) and under the direct control of the laboratory manager</td>
<td>Request forms (closely linked to the test requesting process) including test profiles and problem-based requesting</td>
<td>The laboratory with the involvement of clinicians</td>
<td>Local and national, in particular for problem-based requesting</td>
<td>National laboratory societies</td>
<td></td>
</tr>
<tr>
<td>Patient identification</td>
<td>Laboratory, hospital ward/ outpatient clinic, GP's office</td>
<td>International for principles for identification, with local adaptations</td>
<td>Accreditation bodies</td>
<td>IT resources</td>
<td>EQA organisations</td>
</tr>
<tr>
<td>Sample material, collection, preparation, transportation</td>
<td>Laboratory, hospital ward/ outpatient clinic, GP's office</td>
<td>International for sample materials and their preparation</td>
<td>International and national laboratory societies/organisations Manufactures</td>
<td>Strong opinion leaders, Competition among laboratories</td>
<td>International and national laboratory societies EQA organisations</td>
</tr>
<tr>
<td>Interference, eg. by haemolysis, lipids, bilirubin</td>
<td>Laboratory</td>
<td>International, but method-dependent</td>
<td>International and national laboratory societies/organisations Manufactures</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Analytical Procedures under the direct control of the laboratory</td>
<td>Methods and quality control systems</td>
<td>Laboratory</td>
<td>International</td>
<td>International laboratory organisations (eg. the harmonisation initiative by AACC and standardisation by IFCC)</td>
<td>Manufacturers Disagreement between opinion leaders</td>
</tr>
</tbody>
</table>
A system to get an overview of the possibility to harmonize

1. What to harmonise
   1. The phase and the steps in the phase
   2. Who has the responsibility.

2. Possibility for harmonisation
   1. Likely achievable level
   2. Drivers / facilitators
   3. Barriers
   4. Structures for monitoring the harmonization
Analytical phase

1. What to harmonise
   1. Steps: *Measurement methods*
   2. Responsibility: *The laboratory*

2. Possibility for harmonisation
   1. Likely achievable level: *International*
   2. Drivers: *International lab organisations, regulatory bodies*
   3. Barriers: *Manufacturers, opinion leaders? Money*
   4. Structures for monitoring: *EQA organisations*
International Consortium for Harmonization of Clinical Laboratory Results

- Strategic Partners Group
- Council
- Harmonization Oversight Group
  - Harmonization Implementation Groups
  - Special Working Groups

Secretariat/Host - AACC
Pre-suppositions for EQA organisation to be able to perform monitoring of the harmonization of methods

Commutable control material

One common target value for all methods (either a reference method or a “consensus” method after harmonisation)
Pre (pre) analytical phase

1. What to harmonise
   1. The different steps in the phase: Request form
   2. Responsibility: The laboratory (with involvement of clinicians)

2. Possibility for harmonisation
   1. Likely achievable level: Local / regional
   2. Drivers: National laboratory organisations
   3. Barriers: Opinion leaders/reimbursement/competition among laboratories
   4. Structures: consensus meetings / EQA organisations
Pre-analytical phase

1. What to harmonise
   1. The different steps in the phase: *Stability of tests*
   2. Responsibility: *The laboratory*

2. Possibility for harmonisation
   1. Likely achievable level: *International for method establishment / method dependent / national*
   2. Drivers: *Laboratory organisations*
   3. Barriers: *Reimbursement/Practical issues*
   4. Structures: *EQA organisations*
Likely achievable level of harmonization / stability

International: Agreement on (a) method(s) for examining stability. E.g. CLSI, ISO, IFCC document. What is acceptable variation/quality specifications?

National: Establishing databases on stability of constituents (dependent on methods?) and transport forms.
Monitoring structure / stability

(National) EQA organizations by regular monitoring e.g. acceptable stability times for (different) samples at different laboratories and with user meetings try to discuss this
Review

How to conduct External Quality Assessment Schemes for the pre-analytical phase?

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Abstract

In laboratory medicine, several studies have described the most frequent errors in the different phases of the total testing process, and a large proportion of these errors occur in the pre-analytical phase. Schemes for registration of errors and subsequent feedback to the participants have been conducted for decades concerning the analytical phase by External Quality Assessment (EQA) organizations operating in most countries. The aim of
EQAS and harmonisation of the pre-analytical phase

In principle three different types;

a) collecting information about pre-analytical laboratory procedures

b) Circulation of real samples to collect information about for example interferences that might affect the measurement procedure

c) register actual laboratory errors and relate these to quality indicators.

Post-analytical phase

1. What to harmonise
   1. The different steps in the phase: Reflex/reflective testing
   2. Responsibility: The laboratory together with clinicians

2. Possibility for harmonisation
   1. Likely achievable level: Local
   2. Drivers: National Laboratory organisations/Competition between laboratoratories
   3. Barriers: Laboratory resources / Opinion leaders / reimbursement systems
   4. Structures: National lab organisations/ EQA organisations
Reflex/reflective testing can be harmonised within certain areas or countries, but is likely to be difficult to achieve on an international scale as the disease spectrum and prevalence of disease vary among countries.

Accreditation bodies have the potential to be facilitators for harmonisation of verification procedures, whereas national laboratory societies could be drivers for implementing harmonised routines for reflex and/or reflective testing.
Post-analytical phase

1. What to harmonise
   1. The different steps in the phase: *Units / reference intervals*
   2. Responsibility: *The laboratory (together with clinicians)*

2. Possibility for harmonisation
   1. Likely achievable level: *national / international*
   2. Drivers: *National/International Laboratory organisations*
   3. Barriers: *Opinion leaders*
   4. Structures for monitoring: *EQA organisations*
What are the biggest challenges concerning the harmonization?

- To achieve a consensus (local, national, international, between medical disciplines) about how “it should be done”
- To transform the EQA organizations to meet the challenge
- To have accreditation bodies ask for the results of such EQA schemes
At this point of time, the laboratory profession has a golden opportunity to view outwards and influence those parts of the total testing process that traditionally have not been directly under our control. This may be challenging as the farther we move “out” from the central laboratory and the analytical process, the more we have to fight for our view among other professions and show how our input is essential for best practise
Thank you
So – what should I talk about

Is it possible to harmonize the different phases within- and between countries, to what stage can harmonization be achieved – and who should do it?
Challenges for laboratory medicine

This may be challenging as the farther we move “out” from the central laboratory and the analytical process, the more we have to fight for our view among other professions and show how our input is essential for best practise.

- And this can probably often explain why we retract to our reference limits and control rules.
To be able to harmonize, we have to achieve agreement or consensus and we have to establish structures where we can monitor what we are doing.

Can laboratory medicine do this – for some of the “phases” we need other medical specialities?
Analytical phase

1. What to harmonise
   1. Steps: Internal quality control (and how to handle it)
   2. Responsibility: The laboratory

2. Possibility for harmonisation
   1. Likely achievable level: National / International
   2. Drivers: International lab organisations, regulatory bodies
   4. Structures for monitoring: EQA organisations
Pre-analytical phase

1. What to harmonise
   1. The different steps in the phase: Interferences
   2. Responsibility: The laboratory

2. Possibility for harmonisation
   1. Likely achievable level: International / method dependent
   2. Drivers: Laboratory organisations
   3. Barriers:
   4. Structures: EQA organisations
How to handle results within the laboratory

Example: post-analytical haematology
Registration of procedures

Example: registration by questionnaire (web-based). Done for e.g. clinical chemistry procedures, thresholds for hemolysis.

WEQAS: 4 times a year
Circulation of real samples

Circulation of hemolytic, icteric or other samples

Post-analytical phase

1. What to harmonise
   1. The different steps in the phase: Report forms
   2. Responsibility: The laboratory (together with clinicians)

2. Possibility for harmonisation
   1. Likely achievable level: national
   2. Drivers: National/International Laboratory organisations/regulatory bodies
   3. Barriers: It resources?:
   4. Structures for monitoring: EQA organisations/National societies