Quality Assurance of the pre-analytical phase

Ana-Maria Šimundić

DEPARTMENT OF MEDICAL LABORATORY DIAGNOSTICS
CLINICAL HOSPITAL SVETI DUH, ZAGREB, CROATIA
Why pre-analytical EQA?
Types of pre-analytical EQA?
Benefits and challenges?
Some examples
Why pre-analytical EQA?
Preanalytical phase

- is the most common source of errors
- huge variations in practices and policies
  - between continents
  - between countries
  - between labs
  - between individuals
CONCLUSIONS: Laboratory professionals in Croatia have a positive attitude towards the importance of patient preparation for laboratory testing. However, the information for laboratory testing is not standardized and frequently lacks guidance for tests related to TDM, coagulation and endocrinology. This study highlights the need for standardized, updated and evidence-based recommendations for patient preparation in order to minimize the risk for patients.
Are patients well informed about the fasting requirements for laboratory blood testing?

Sanja Kackov\textsuperscript{1}, Ana-Maria Simundic\textsuperscript{2}, Ani Gatti-Dmic\textsuperscript{3}

\textsuperscript{1}Medical biochemistry laboratory, Policlinic Bonifarm, Zagreb, Croatia  
\textsuperscript{2}University Department of Chemistry, Medical School University Hospital Sestre Milosrdnice, Zagreb, Croatia  
\textsuperscript{3}Medical biochemistry laboratory, Public Health Centre Zagreb-Centar, Zagreb, Croatia

**Table 1.** The questionnaire used in the survey about how patients are informed of proper preparation for phlebotomy (N = 150).

<table>
<thead>
<tr>
<th>Question</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>4.2. When did you consume meal last time?</strong></td>
<td></td>
</tr>
<tr>
<td>- the last meal consumed 12 hours before</td>
<td>90 (60)</td>
</tr>
<tr>
<td>- the last meal consumed 10 hours before</td>
<td>32 (21)</td>
</tr>
<tr>
<td>- the last meal consumed 18 hours before</td>
<td>2 (1)</td>
</tr>
<tr>
<td>- coffee or tea in the morning</td>
<td>17 (12)</td>
</tr>
<tr>
<td>- the last meal prior to phlebotomy</td>
<td>9 (6)</td>
</tr>
<tr>
<td><strong>4.4. When did you consume liquid last time (water, juice, coffee, etc.)?</strong></td>
<td></td>
</tr>
<tr>
<td>- without fluid in the morning</td>
<td>69 (46)</td>
</tr>
<tr>
<td>- with water in the morning</td>
<td>57 (38)</td>
</tr>
<tr>
<td>- coffee or tea in the morning</td>
<td>21 (14)</td>
</tr>
<tr>
<td>- juice in the morning</td>
<td>2 (1)</td>
</tr>
<tr>
<td>- milk in the morning</td>
<td>1 (1)</td>
</tr>
</tbody>
</table>
There is a large heterogeneity in Europe!

Only a few countries have guidelines (7/28)

Phlebotomy is performed by medical and nonmedical personnel

different level of education and life long training
Compliance of blood sampling procedures with the CLSI H3-A6 guidelines: An observational study by the European Federation of Clinical Chemistry and Laboratory Medicine (EFLM) working group for the preanalytical phase (WG-PRE)

Conclusions: The level of compliance of phlebotomy procedures with the CLSI H3-A6 guidelines in 12 European countries was found to be unacceptably low. The most critical steps in need of immediate attention in the investigated countries are patient identification and tube labelling.
The quality of the extra-analytical phase of laboratory practice in some developing European countries and Mexico – a multicentric study

<table>
<thead>
<tr>
<th>Question</th>
<th>n</th>
<th>Never, %</th>
<th>Rarely, %</th>
<th>Often, %</th>
<th>Always, %</th>
<th>Overall score</th>
</tr>
</thead>
<tbody>
<tr>
<td>I centrifuge already coagulated samples shorter than required</td>
<td>404</td>
<td>66</td>
<td>17</td>
<td>10</td>
<td>7</td>
<td>3.42</td>
</tr>
<tr>
<td>I do not accept the sample for analysis unless the tube containing anticoagulant is filled up to the mark</td>
<td>386</td>
<td>13</td>
<td>19</td>
<td>9</td>
<td>59</td>
<td>3.13</td>
</tr>
<tr>
<td>If the potassium concentration in a slightly haemolytic serum is normal, I will not request new blood sampling</td>
<td>263</td>
<td>25</td>
<td>20</td>
<td>34</td>
<td>21</td>
<td>2.50</td>
</tr>
<tr>
<td>I centrifuge blood samples for serum for at least 10 min at 3500 rpm</td>
<td>368</td>
<td>20</td>
<td>6</td>
<td>11</td>
<td>63</td>
<td>3.17</td>
</tr>
<tr>
<td>I run the complete blood count from a slightly coagulated sample, carefully observing that the coagulum will not be aspirated</td>
<td>377</td>
<td>66</td>
<td>7</td>
<td>2</td>
<td>25</td>
<td>3.13</td>
</tr>
<tr>
<td>If the samples for the potassium measurement are even slightly haemolytic, I will request new sampling</td>
<td>359</td>
<td>8</td>
<td>23</td>
<td>16</td>
<td>53</td>
<td>3.14</td>
</tr>
</tbody>
</table>
Blood Glucose Determination: Effect of Tube Additives

Giuseppe Lippi*, Mads Nybo†, Janne Cadamuro‡, Joao T. Guimaraes§, Edmée van Dongen-Lases#, Ana-Maria Simundic**

Fig. 3  Variation of glucose concentration in samples stored uncentrifuged for 0.5–4 h at room temperature. KOx, potassium oxalate; NaF, sodium fluoride.
Opinion Paper

Ana-Maria Simundic*, Michael P. Cornes, Kjell Grankvist, Giuseppe Lippi, Mads Nybo, Ferruccio Ceriotti, Elvar Theodorsson and Mauro Panteghini on behalf of the European Federation for Clinical Chemistry and Laboratory Medicine (EFLM)

Colour coding for blood collection tube closures – a call for harmonisation
Standardizing in vitro diagnostics tasks in clinical trials: a call for action

Giuseppe Lippi\textsuperscript{1,2}, Ana-Maria Simundic\textsuperscript{1,3}, Leocadio Rodrigues-Manas\textsuperscript{4}, Patrick Bossuyt\textsuperscript{5}, Giuseppe Banfi\textsuperscript{6}

Patients should receive the same level of care across Europe!

Standardization of preanalytical practices is essential!
Standardization

Formulation, publication, and implementation of guidelines, rules, and specifications for common and repeated use, aimed at achieving optimum degree of order or uniformity in a given context, discipline, or field.
Harmonization

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 interchangeably.

Clinical and Laboratory Standards Institute
Harmonization in laboratory medicine: the complete picture

- Harmonization in laboratory medicine is mandatory.
- Standardization and harmonization projects should deal with all steps of the total testing process: pre-, analytical and post-analytical phase.
- Initiatives aiming to improve harmonization of laboratory test results have an ethical dimension.
- Main purpose is to provide reliable information that, in turn, should assure optimal care for patients in a global world.
External quality assessment (EQA)

- provides confidence that the results are comparable.
- is a tool for:
  - achieving comparability and reducing variation
  - identifying gaps and targeting training needs
  - monitoring laboratory performance over time and maintaining quality
External quality assessment programmes should, as far as possible, provide clinically relevant challenges that mimic patient samples and have the effect of checking the entire examination process, including pre- and post-examination procedures.
Types of pre-analytical EQA?
How to conduct External Quality Assessment Schemes for the pre-analytical phase?

Gunn B.B. Kristensen¹*, Kristin Moberg Aakre¹,², Ann Helen Kristoffersen²,³, Sverre Sandberg²,³

¹The Norwegian EQA Program (NKK), Bergen, Norway
²Laboratory of Clinical Biochemistry, Haukeland University Hospital, Bergen, Norway
³Noklus (Norwegian Centre for Quality Improvement of Primary Care Laboratories), University of Bergen, Bergen, Norway

- Type I: Registration of procedures
- Type II: Circulation of samples simulating errors
- Type III: Registration of errors/adverse events
Type I preanalytical EQA

Surveys (questionnaires)
- questions about policies and procedures,
- preanalytical cases

Advantages
- low cost
- easy to distribute widely
### Table 1. Examples of ongoing pre-analytical EQAS.

<table>
<thead>
<tr>
<th>Method</th>
<th>Pre-analytical issues studied</th>
<th>Frequency</th>
<th>Performed by</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Type I. Registration of procedures</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Registration of procedures via web-based multiple choice questionnaire</td>
<td>Clinical chemistry: Hemolysis, stability of samples (2011)</td>
<td></td>
<td>Norwegian Clinical Chemistry EQA program (NKK)</td>
</tr>
<tr>
<td></td>
<td>Hemostasis testing: Phlebotomy, sample handling and sample acceptance (2012)</td>
<td>1 x year</td>
<td>Not published</td>
</tr>
<tr>
<td></td>
<td>Glucose: Sample handling and sample treatment (2013)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Registration of procedures via web-based multiple choice questionnaire</td>
<td>Hemostasis testing</td>
<td>2 x year</td>
<td>ECAT/INSTAND 2011 (25)</td>
</tr>
<tr>
<td>Clinical case-based European EQAS covering pre-analytical, analytical and post-analytical phase. Five sets of multi-specimen samples</td>
<td>Porphyria: Case history based test ordering</td>
<td>2 x year</td>
<td>Norwegian Porphyria Centre (NAPOS)/The European Porphyria Network (EPNET) (26)</td>
</tr>
<tr>
<td>Registration of procedures via web-based multiple choice questionnaire</td>
<td>5 general pre- and post-analytical questions, 5 questions within specific disciplines (i.e. coagulation, hematology, immunology, microbiology)</td>
<td>2 x year</td>
<td>* Quality Control Center Switzerland (CSCO)</td>
</tr>
<tr>
<td>Registration of procedures via multiple choice questionnaire</td>
<td>Urine chemistry, clinical chemistry</td>
<td>4 x year</td>
<td>* WEOAS</td>
</tr>
<tr>
<td>Registration of procedures via web-based multiple choice questionnaire</td>
<td>Hematology, sample handling</td>
<td>1 x year</td>
<td>* INSTAND</td>
</tr>
</tbody>
</table>
The Prenanalytical EQA Survey is FREE to all biorepositories.

This is a Preanalytical External Quality Assessment scheme for the pre-analytical phase in biorepositories. It is based on collection of information about pre-analytical biorepository procedures (Biochemia Medica 2014;24:114-122). It has been developed by the ISBER Biospecimen Science Working Group, and approved by the ISBER Education and Training Committee. The scheme is applicable to all biorepositories, both clinical and environmental.
PROCEDURES

2. Do you have written procedures to define default pre-analytical conditions?

"Default": A particular setting for a pre-analytical variable that is assigned in a standard way and remains in effect unless canceled or modified by the operator (e.g. default tissue fixation time being 24 hrs)

- Yes
- No

3. Do you have written procedures to record pre-analytical variables? (e.g. SPREC or in any other way)?

- Yes
- No

4. Do you have written procedures to track and report pre-analytical non-conformities?

"Non-Conformities": any procedure or step in a procedure which does not conform to the standard procedure

- Yes
- No

5. Do you have written procedures to track temperature excursions during storage?

- Yes
- No
Type I Preanalytical EQA in Croatia – the origins

Učestalost pojedinih postupaka izvananalitičke faze laboratorijske dijagnostike u Hrvatskoj - presječno anketno istraživanje

Self reported routines and procedures for the extra-analytical phase of laboratory practice in Croatia - cross-sectional survey study

Lidija Bilić-Zulle1,2, Ana-Maria Šimundić3, Vesna Šupak Smolčić3, Nora Nikolac3, Lorena Honović4

Type I Preanalytical EQA in Croatia – the origins

<table>
<thead>
<tr>
<th>Question</th>
<th>N</th>
<th>Never (%)</th>
<th>Rarely (%)</th>
<th>Often (%)</th>
<th>Always (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Questions on criteria of sample acceptance</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Already coagulated samples are centrifuged shorter than required.</td>
<td>143</td>
<td>64</td>
<td>26</td>
<td>8</td>
<td>2</td>
</tr>
<tr>
<td>The sample for analysis will not be accepted, unless the tube containing anticoagulant is filled up to the mark.</td>
<td>143</td>
<td>4</td>
<td>26</td>
<td>20</td>
<td>50</td>
</tr>
<tr>
<td><em>If potassium concentration in a slightly hemolytic serum is normal, new blood sampling will not be requested.</em></td>
<td>143</td>
<td>29</td>
<td>29</td>
<td>24</td>
<td>18</td>
</tr>
<tr>
<td>Blood samples for serum are centrifuged at least 10 minutes at 3500 rpm.</td>
<td>144</td>
<td>4</td>
<td>0</td>
<td>9</td>
<td>87</td>
</tr>
<tr>
<td><em>Complete blood cells count from a slightly coagulated sample will be performed carefully observing that the coagulum is not aspirated.</em></td>
<td>140</td>
<td>84</td>
<td>9</td>
<td>2</td>
<td>5</td>
</tr>
<tr>
<td>If the samples for the potassium measurement are even slightly hemolytic, new sampling will be requested.</td>
<td>142</td>
<td>8</td>
<td>21</td>
<td>24</td>
<td>47</td>
</tr>
</tbody>
</table>
Type I Preanalytical EQA in Croatia – the origins

Conclusions:
Results indicate the urgent need for improving activities in the extra-analytical phase, especially phlebotomy procedures. Reinforced education of all the personnel involved, appropriate recording and monitoring of extra-analytical phase is necessary to reach high quality standards.
2014 - First preanalytical EQA

In 2014 - 1 pilot round per year:
- Modul 10 - pre-analytical
- Modul 11 - post-analytical

From 2015 - 3 rounds per year:
- Modul 10 - pre-analytical
- Modul 11 - post-analytical
Preanalytical EQA (2014)

3 preanalytical cases:
- incorrect collection of 24h urine
- incorrect sampling time for the OGTT - prolonged fasting.
- request for potassium in slightly hemolyzed sample

- questions related to sample acceptance criteria
Preanalytical EQA (2014)

- Questions
  - multiple choice
  - only one answer was correct according to current recommendations and standards of good laboratory practice in Croatia.

- Individualized reports:
  - absolute numbers and percentages of respondents.
  - educative comments.
Case 1 – description (2014)

- patient arrives to the lab in the morning (8:00 am).
- creatinine clearance is requested.
- patient brings 24h urine (1500 mL) in a clean plastic bottle.
- patient says that he had collected entire urine with the exception of the first morning urine on the day of arrival to the lab (1 - 2 dL) because the urine container was full.
Possible choices

Please select response which best describes the policy and procedure with a sample in your laboratory:

<table>
<thead>
<tr>
<th>Number of participants (N=151)</th>
<th>Listed responses</th>
<th>Frequency of response: N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>a) the sample is accepted for testing, and the result be issued without note</td>
<td>0 (0)</td>
</tr>
<tr>
<td></td>
<td>b) the sample is not acceptable, but is accepted for testing, and the result be issued with the note</td>
<td>9 (6)</td>
</tr>
<tr>
<td></td>
<td>c) the sample is not acceptable and is not accepted for testing</td>
<td>136 (90)</td>
</tr>
<tr>
<td></td>
<td>d) although the sample is not acceptable, in exceptional situations may be accepted if the user* explicitly requires it</td>
<td>6 (4)</td>
</tr>
</tbody>
</table>

With courtesy of Jasna Leniček Krleža, CROQALM Chair
# RESULTS ANALYSIS AND INTERPRETATION

## CASE 1

<table>
<thead>
<tr>
<th>Listed responses</th>
<th>N= 151</th>
<th>%</th>
<th>Your respond</th>
<th>Preferred response</th>
</tr>
</thead>
<tbody>
<tr>
<td>the sample is accepted for testing, the result be issued without note</td>
<td>0</td>
<td>0.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td>the sample is accepted for testing, the result be issued with the note</td>
<td>9</td>
<td>5.96</td>
<td></td>
<td></td>
</tr>
<tr>
<td>the sample is not acceptable and is not accepted for testing</td>
<td>136</td>
<td>90.07</td>
<td></td>
<td></td>
</tr>
<tr>
<td>although the sample is not acceptable, in exceptional situations may be accepted if the user* explicitly requires it</td>
<td>6</td>
<td>3.97</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*user: physician who requested testing or patient
MODUL: MODUL 10 - PREDANALITIČKA FAZA LABORATORIJSKOG RADA

ANALIZA REZULTATA

U modulu 10 sudjelovalo je 161/180 laboratorija što iznosi 89,44%.
U prvom slučaju poželjni odgovor c) odabralo je 136/151 = 90,07% laboratorija. Pravilno prikupljanje uzorka, koje uključuje cjelokupnu količinu mokraće izmokrenu unutar 24 sata, neophodno je za izdavanje rezultata za klirens kreatinina. Odstupanje od definiranog protokola sakupljanja 24-satne mokraće može dovesti do značajnih varijacija u rezultatu.
U drugom slučaju poželjni odgovor c) odabralo je 134/160 = 83,75% laboratorija. Prema svim važećim preporukama stručnih društava, OGTT se izvodi ujutro između 7.00 i 9.00 sati. Izvođenje ovog testa nakon produljenog gladovanja može dovesti do značajnih varijacija u rezultatu.
U trećem slučaju poželjni odgovor c) odabralo je 134/159 = 85,53% laboratorija. Kalij je jedan od parametara čija je koncentracija promijenjena čak i pri najmanjoj hemolizii uzorka. S obzirom da stupanj hemolize nije u linearnom odnosu s promjenom koncentracije kalija, nemoguće je iz koncentracije slobodnog hemoglobina procijeniti kolika će biti promjena koncentracije kalija. Stoga se preporučuje odbacivanje hemolitičkog uzorka za mjerenje koncentracije kalija. Koncentracija kalija u hemolitičnom uzorku je nepouzdana.
Za postupanje s hemolitičnim uzorcima, većina laboratorija koristi preporuke HKMB (134/161 = 83,23%), a tek manji broj preporuke proizvođača (24/161 = 14,91%) ili vlastite rezultate verifikacije interferencija (2/161 = 1,24%). Za neke parametre (K, LD, AST) interferencija hemolize neovisna je o metodi, dok su za pojedine parametre (kolesterol, trigliceridi, bilirubin, magnezij) jačina i stupanj interferencije ovisni o uporabljenoj reagensu. Utjecaj hemolize na mjerenje koncentracije ovakvih parametara različit je kod različitih proizvođača reagensa.
Rezultati prvog modula za predanalitičku fazu laboratorijskog rada pokazuju vrlo dobro slaganje postupaka s važećim preporukama i stručnim standardima. Laboratoriji se potiču da postupanje s uzorcima s interferencijama prilagode specifičnim metodama koje koriste u laboratoriju te da za granične vrijednosti za odbacivanje nesukladnih uzoraka koriste podatke dobivene od proizvođača. Zbog mogućeg neslaganja deklariranih vrijednosti i rezultata dobivenih u laboratoriju, poželjno je napraviti verifikaciju deklariranih podataka.

With courtesy of Jasna Leniček Krleža, CROQALM Chair
Case 3 – description (2014)

The laboratory has received the blood sample with a request for serum potassium measurement. After centrifugation, sample is slightly hemolyzed (free hemoglobin concentration of 0.5 g/L; Figure 1: tubes No. 3).

With courtesy of Jasna Leniček Krleža, CROQALM Chair
Please select response which best describes the policy procedure with a sample in your laboratory:

<table>
<thead>
<tr>
<th>Number of participants (N=159)</th>
<th>Frequency of response: N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Listed responses:</td>
<td></td>
</tr>
<tr>
<td>a) the sample is accepted for testing, and the result be issued without notice</td>
<td>0 (0)</td>
</tr>
<tr>
<td>b) the sample is not acceptable, but is accepted for testing, and the result be issued with the note</td>
<td>15 (9)</td>
</tr>
<tr>
<td>c) the sample is not acceptable and is not accepted for testing</td>
<td>136 (86)</td>
</tr>
<tr>
<td>d) although the sample is not acceptable, in exceptional situations may be accepted if the user* explicitly requires it</td>
<td>8 (5)</td>
</tr>
</tbody>
</table>

With courtesy of Jasna Leniček Krleža, CROQALM Chair
Preanalytical EQA (2015)

Compliance with National recommendation for venous blood sampling (published 2014):

- 1/2015 - consumables, materials and equipment
- 2/2015 - patient identification
- 3/2015 – venous blood sampling
- 1/2016 – sample transport and delivery
Preanalytical EQA (1/2015)
Consumables, materials and equipment

- SOP for blood sampling
- Needles (multiple sizes)
- Wingset needles
- Safe-sharp needles
- Tubes (multiple volumes)
- Sterile pads
- Sterile gloves
- Single use holders
- Single use tourniquet
- Phlebotomy chair
- Safe waste disposal

Preanalytical EQA (2/2015)
Patient identification

Preanalytical EQA (3/2015)

Blood sampling

- Fasting status is checked
- Tourniquet always used
- Gloves put before the tourniquet
- Wait for 30 seconds for alcohol to dry
- If sampling not successful, blood is drawn without vacuum
- Tourniquet is released when the blood started to flow
- Coagulation tube is drawn prior to serum tube
- Sampling not done if patient not fasting
- No

Type II preanalytical EQA

- circulation of samples with some kind of error
  - lipemic, hemolyzed, icteric sample
  - drug interference
  - EDTA contamination
  - wrong additive (heparin instead of clot activator)
- could be accompanied with a case history
## Type II preanalytical EQA

<table>
<thead>
<tr>
<th>Type II. Circulation of samples simulating errors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Circulate samples for extraction of RNA/DNA</td>
</tr>
<tr>
<td>Sample preparation for DNA and RNA testing</td>
</tr>
<tr>
<td>SPIDIA-DNA, 2012</td>
</tr>
<tr>
<td>SPIDIA-RNA, 2011</td>
</tr>
<tr>
<td>European Commission (EC)</td>
</tr>
<tr>
<td>(33, 34)</td>
</tr>
<tr>
<td>Circulate samples</td>
</tr>
<tr>
<td>Sample indices – lipemic, icteric, hemolysis</td>
</tr>
<tr>
<td>index</td>
</tr>
<tr>
<td>WEQAS</td>
</tr>
</tbody>
</table>

- Nordic hemolysis project
- Croatian society (CROQALM)
143 laboratories participated (response rate was 97%):
- 32 from Denmark,
- 25 from Finland,
- 4 from Iceland,
- 53 from Norway
- 29 from Sweden.

Four samples with different degrees of hemolysis were distributed to the laboratories (0, 100, 200 and 400 mg Hb/dL).
The laboratories were asked to provide their H-index (Hb concentration) value and measure 15 different clinical chemistry components in duplicate:

- Alkaline phosphatase (ALP), bilirubin (total), calcium, creatine kinase (CK), chloride (Cl), cobalamin, folate, free thyroxine (FT4), gamma glutamyltransferase (GGT), glucose, lactate dehydrogenase (LDH), potassium, sodium, thyroid-stimulating hormone (TSH) and uric acid.

Labs were also asked to answer some questions concerning how hemolyzed samples were handled in the laboratory.
Results

Participating laboratories differ in actions taken upon the analytical results for most of the components (reject, reject with comment, report or report with comment).
A PRE-ANALYTICAL EQA SCHEME FOR SAMPLE INTEGRITY: A WEQAS STUDY TO MONITOR THE EFFECTIVENESS OF SERUM INDICES

Thomas MA, Davies G, Jones S, Davison L, Phillips J
WEQAS, Cardiff and Vale University Health Board, Unit 6, Parc Ty Glas, Llanishen, Cardiff, UK, CF14 5DU

Corresponding author: Annette.thomas2@wales.nhs.uk

Background: Whilst most EQA schemes focus on the data counting of the number of rejected samples, WEQAS has developed a programme to evaluate the laboratory’s ability to detect unsuitable samples and assess their testing protocols for the analytes affected.

Materials and methods: Samples were distributed every 3 months with varying degrees of lipemia, hemolysis and icterus over a 4 year period. Two matched pools were distributed, one containing the interferent and the other containing normal physiological levels. Participants were asked to provide their serum indices value and to report results as they would a patient sample. The data for the two matched samples was also compared with a reference method wherever possible to ascertain the degree of analytical interference.

Results: For the icterus sample, 220 laboratories returned results, 57 provided serum indices and 41 provided additional comments indicating as to whether they would have reported the result on a patient sample. Of these, the majority stated that they would not report total protein, creatinine or GGT.

For the lipemic sample, 111 laboratories provided serum indices and 61 participants provided additional comments. Of these, the majority stated that they would not report ALT and AST with 8 laboratories adding further lipid investigations.

For the hemolyzed sample, 144 laboratories returned results, 109 participants provided additional comments that they would not report Potassium, ALT, AST CK, LDH and ALP. Fifteen stated that they would not have provided any results.

Conclusions: There appears to be little harmonization of reporting for serum indices even within users of the same instrument. It is important that laboratories are aware of potential interferences in their assays, are aware of which analytes could be affected, have the ability to detect the potential interferences and have systems in place to ensure the accuracy of results when these interferences are present.
SPIDIA

- funded by the European Commission, 4 year project
- project aim:
  - to develop quality guidelines and tools for in vitro molecular diagnostics
  - to standardize the preanalytical process (transport and handling)
  - the implementation of EQA for the collection, transport and processing of blood samples for RNA and DNA-based analyses is an essential part of this project
Labs receive blood samples and are asked to do:
- DNA or RNA extraction
- provide details about the reagents and protocols used for the extraction

Extracted DNA and RNA samples are evaluated for purity, yield, integrity, stability, and the presence of interfering substances inhibiting molecular assays.

All participants received a report comparing the performance of the DNA and RNA they submitted to that of the other participants.
A. Purity and Concentration of DNA1, DNA2 and DNA3 (pre-extracted DNAs)

A.1 Spectrophotometric data provided by your lab

<table>
<thead>
<tr>
<th></th>
<th>260nm</th>
<th>280nm</th>
<th>320nm</th>
<th>Purity</th>
<th>Concentration (ng/μl)</th>
<th>Dilution factor</th>
</tr>
</thead>
<tbody>
<tr>
<td>DNA1</td>
<td>1.397</td>
<td>0.783</td>
<td></td>
<td>1.78</td>
<td>69.8</td>
<td>1</td>
</tr>
<tr>
<td>DNA2</td>
<td>0.389</td>
<td>0.240</td>
<td></td>
<td>1.62</td>
<td>19.4</td>
<td>1</td>
</tr>
<tr>
<td>DNA3</td>
<td>1.817</td>
<td>1.373</td>
<td></td>
<td>1.32</td>
<td>90.8</td>
<td>1</td>
</tr>
</tbody>
</table>

A.2 Your lab (●) versus overall distribution (N=172) – Purity

In the figures the blue lines represent the Action Limits (ALs) and the gray lines represent the Warning Limits (WLs).

DNA1: Lower AL=1.45; Upper AL=2.01; Lower WL=1.71; Upper WL=1.95

DNA2: Lower AL=1.09; Upper AL=2.35; Lower WL=1.45; Upper WL=2.08

DNA3: Lower AL=1.17; Upper AL=1.50; Lower WL=1.30; Upper WL=1.42

in control

www.spidia.eu
Preanalytical EQA (2017-2018)

How do labs treat lipemic samples?
- 1/2017 - chemistry
- 2/2017 - hematology
- 3/2017 – coagulation

Sample spiked with Intralipid

How do labs treat icteric samples?
- 1/2018 – chemistry
- 2/2018 – coagulation
- 3/2018 - hematology

Sample spiked with bilirubin

(data not published)
How do you detect degree of icterus in chemistry samples?

<table>
<thead>
<tr>
<th>Answer Choices</th>
<th>Responses</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Vizualno</strong></td>
<td>67.08%</td>
</tr>
<tr>
<td><strong>Mjerenje na automatskom analizatoru</strong></td>
<td>32.92%</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td>161</td>
</tr>
</tbody>
</table>
How do you detect degree of icterus in coagulation samples?

Answered: 148   Skipped: 1

Visually

HIL indices

(data not published)
Estimate the degree of icterus in the (chemistry) sample.

Answered: 157   Skipped: 5

- Not icteric
- Mildly icteric
- Icteric
- Severely icteric (data not published)

<table>
<thead>
<tr>
<th>ANSWER CHOICES</th>
<th>RESPONSES</th>
</tr>
</thead>
<tbody>
<tr>
<td>uzorak nije ikteričan</td>
<td>1.91%</td>
</tr>
<tr>
<td>uzorak lagano ikteričan</td>
<td>8.92%</td>
</tr>
<tr>
<td>uzorak ikteričan</td>
<td>69.43%</td>
</tr>
<tr>
<td>uzorak izrazito ikteričan</td>
<td>19.75%</td>
</tr>
</tbody>
</table>
Given the estimated degree of icterus, please state what would you do with the request for creatinine in the sample.

Answered: 157    Skipped: 5

- Report without a comment
- Report with a comment
- Report after sample treatment
- Report after sample treatment, with a comment
- I would not report a result

(data not published)
Challenges in Type II EQA

- Same as analytical EQA (sample stability, commutability, homogeneity, etc.)
- Requires dedicated and competent personnel and some resources (equipment, samples, facilities)
- Requires expertise (how to produce unsuitable samples?)
- Difficult to mimic real life preanalytical problems on a large scale
- Only a very limited number of preanalytical problems can be explored (not to be used on a regular basis)
- Response bias (participants know they are receiving „preanalytical samples“)
Type III preanalytical EQA

- registration of errors/adverse events
  - labs report their data regularly over time
  - standardized system of reporting
## Type III preanalytical EQA

<table>
<thead>
<tr>
<th>Registration of errors/adverse events</th>
<th>O-Track (since 1998, 1 x year, ongoing) programs, registration of error rates</th>
<th>Patient/sample identification, specimen handling/preparation, specimen acceptability, customer satisfaction</th>
<th>4 x year</th>
<th>College of American Pathologists (CAP) (39)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Registration of rejection of samples</td>
<td>Registration of the rejection rate and causes for rejecting the samples during 1 month or 100 rejections</td>
<td>2 x year</td>
<td>Committee for the Quality of the Extra-analytical phase (started within The Spanish Society of Clinical Chemistry and Molecular Pathology (SEQC) in 1998 (41)</td>
<td></td>
</tr>
<tr>
<td>Registration of key incidents which represent either the most frequent or most serious incident</td>
<td>Patient identification, incorrect patient preparation, phlebotomy, sample preparation/handling and sample acceptability</td>
<td>4 x year</td>
<td>Key Incident Monitoring and Management Systems Quality Assurance (KIMMS QA) 2009 (43).</td>
<td></td>
</tr>
</tbody>
</table>

- UK experience
- IFCC Working Group on Laboratory errors and patient safety (WG-LEPS)
Monitoring and reporting of preanalytical errors in laboratory medicine: the UK situation

Michael P Cornes¹,², Jennifer Atherton²,³, Ghazaleh Pourmahram²,⁴, Hazel Borthwick²,⁵, Betty Kyle²,⁶, Jamie West²,⁷ and Seán J Costelloe²,⁸

Responses indicate that:

- 20% of laboratories do not use automated serum indices.
- 34.5% of laboratories do not routinely monitor any preanalytical quality indicators.
- 91.8% of laboratories are interested in the establishment of an EQA scheme to allow interlaboratory comparisons of preanalytical errors.
Monitoring and reporting of preanalytical errors in laboratory medicine: the UK situation

Michael P Cornes¹,², Jennifer Atherton²,³, Ghazaleh Pourmahram²,⁴, Hazel Borthwick²,⁵, Betty Kyle²,⁶, Jamie West²,⁷ and Seán J Costelloe²,⁸
Challenges of Type III EQA

- results between different schemes not comparable due to the:
  - differences in the reporting system
  - different definitions of errors
- requires substantial amount of time and dedicated personnel
- reporting potentially not reflecting the real life (underreporting)
Benefit of Type III EQA

- offers practical and effective method to monitor preanalytical errors over time and compare with other labs
- promotes a continuous improvement to the benefit of the patient
Conclusions 1/3

- EQA is used to assess the degree of comparability of preanalytical practices

- Various EQA
  - offer different benefits
  - have different challenges

- all types of EQA are useful and complementary
  - should be used together
Conclusions 2/3

- EQA is valuable tool only if there is a system in place for:
  - analysing EQA failures
  - implement corrective and preventive actions
  - monitor changes over time
Conclusions 3/3

- National EQA schemes are advisable as they will more likely target local needs

- Responsibility:
  - National societies
  - Laboratories
Acknowledgments
5th EFLM Conference on Preanalytical Phase
Preanalytical challenges - time for solutions

Save the date!

www.preanalytical-phase.org