The role of EQA in Traceability

Tony Badrick
What is the soft drink named after a drug?
Seven-Up
Settles the Stomach
For Hospital or home use.

LITHIATED LEMON SODA

The added citrates neutralize free acid. The sugar is inverted...burns clean. 7-Up is more than a mixer...It blends out the harsh features. Dispels hangovers...takes the "ouch" out of grouch.

Slenderizing

PRINTED IN U.S.A.
COME IN

“Have a Coke”

HELLO...

P. S.
Everybody likes to shorten words. Abbriviation is a natural use of language. You have “Coke,” the friendly abbreviation for the trade mark “Coca-Cola.” On every hand, I tell the story in a picture you have no often heard in words.
Goal of Pathology Testing

• Provide useful information for the formulation of the correct clinical decision

• Production of accurate and equivalent results, regardless of laboratory or analytical system used to produce them

• Need for each measurand, a reference measurement system (methods and materials) plus a clinically acceptable level of MU
Traditional Role of EQA

• Identification of Poorly Performing Laboratories

• Identification of Poorly Performing Methods
Effect of Participating in a Quality Improvement System over Time for Point-of-Care C-Reactive Protein, Glucose, and Hemoglobin Testing

Tone Bukve,¹ Anne Stavelin,¹ and Sverre Sandberg¹,²,³

**BACKGROUND:** Users of point-of-care testing (POCT) in Norway participate in a quality improvement system that includes education and guidance in safe laboratory management along with participation in external quality assurance schemes (EQAS).

**CONCLUSIONS:** The analytical quality of CRP, glucose, and Hb testing is improved by systematic participation in a quality improvement system over time.

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Seven Q-Tracks Monitors of Laboratory Quality
Drive General Performance Improvement
Experience From the College of American Pathologists Q-Tracks Program
1999–2011

Figure 1. The outpatient order-entry error rate monitor presents errors as percentages of outpatient orders entered. The top line (dash-dotted) traces the error rates of subscribers starting with more than 15% errors, the solid line follows the overall average of all participants, the dotted line charts performance of participants starting in the median 2% to 15% range, and the bottom dashed line maps performance of participants starting with less than 2% errors.

Figure 2. The monitor for identification band (ID) defects presents encounters with absent or defective ID bands as percentages of events in which ID bands were examined. The top line (dash-dotted) traces defect rates found by subscribers starting with more than 15% defects per examination events, the solid line follows the overall average of all participants, the dotted line charts performance of participants starting in the median 2% to 15% range, and the dashed line at the bottom maps performance of participants starting with less than 2% errors.
The standardization journey and the path ahead

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Email: greg.miller@vcuhealth.org.

Abstract: Standardization of clinical laboratory test results has progressed through several stages. External quality assessment (EQA) identified that results were not equivalent in different laboratories in the 1950s. Approaches to use the same methods were promoted in the 1960s and the challenges recognized during the 1970s as in vitro diagnostics manufacturers introduced a variety of technologies to meet the demand for clinical laboratory testing services. Hierarchies of national reference systems were developed in the 1980–1990 period that were hampered by inadequate understanding of the importance of commutable reference materials both for use as calibrators and for EQA. Standards for metrological traceability were developed by the International Organization for Standardization in the 2000s that provided a global approach for establishing robust standardization for approximately 100 measurands. The limitations of non-commutable reference materials became widely appreciated in the 2000s. In 2010 and going forward, laboratory medicine recognized the need for harmonization approaches for the large number of measurands for which higher order certified reference materials and reference measurement procedures are not available. Metrological traceability to certified reference materials and reference measurement procedures remains the first choice when technologically feasible. Metrological traceability to an international harmonization protocol provides an alternative when no other approach is realistically feasible. Achieving equivalent results among different medical laboratory measurement procedures remains an important goal to enable appropriate medical decisions based on laboratory results and decision values included in clinical practice guidelines.

Keywords: Harmonization; metrological traceability; standardization
Figure 1 Timeline for key developments in standardization and harmonization of medical laboratory results. AACC, American Association for Clinical Chemistry; CAP, College of American Pathologists; CDC, Centers for Disease Control and Prevention; CRM, Certified Reference Material; EQA, external quality assessment; EU, European Union; FDA, Food and Drug Administration; IFCC, International Federation for Clinical Chemistry and Laboratory Medicine; ISO, International Organization for Standardization; NBS, National Bureau of Standards; NRSL, National Reference System for the Clinical Laboratory; RMP, reference measurement procedure; USA, United States of America.
RESPONSIBILITY

Metrological traceability: an unbroken chain of calibrations from a clinical sample result to a higher order reference system component (ISO 17511)

SI unit

Certified reference material (pure substance)

Primary CRM in solution

Certified reference material (matrix-based and commutable with clinical samples)

Manufacturer’s working calibrator (master lot)

End-user calibrator

Clinical sample result

Reference measurement procedures to characterize CRM (e.g. mass balance)

Reference measurement procedure (e.g. gravimetry)

Reference measurement procedure (e.g. IDMS)

Manufacturer’s selected measurement procedure

Manufacturer’s standing measurement procedure

End-user IVD medical device
As of the start of 2015 the database lists 295 reference materials for 162 analytes, 170 reference measurement procedures for 79 analytes and 130 reference measurement services for 39 analytes.
JCTLM Database content

- **Vitamins and Micronutrients**: 9 entries
- **Proteins**: High-Purity materials - 7 entries, Matrix Materials - 18 entries
- **Nucleic Acids**: High-Purity materials - 9 entries, Matrix Materials - 1 entry
- **Non-Peptide Hormones**: High-Purity materials - 12 entries, Matrix Materials - 11 entries
- **Non-Electrolyte Metals**: High-Purity materials - 58 entries
- **Metabolites and Substrates**: High-Purity materials - 53 entries, Matrix Materials - 33 entries
- **Enzymes**: High-Purity materials - 6 entries, Matrix Materials - 6 entries
- **Electrolytes**: High-Purity materials - 15 entries, Matrix Materials - 21 entries
- **Drugs**: High-Purity materials - 12 entries, Matrix Materials - 19 entries
- **Coagulation Factors**: High-Purity materials - 2 entries
- **Blood Groupings**: High-Purity materials - 3 entries

**Total entries**: 293
Traceability in EQA

• All EQA results are traceable, it is just a matter of what to.

• For many the way the EQA works is to answer the question (is my X analyser working like an X analyser should). This is traceability to the X analyser group.

• If your reference interval and clinical decision points come from other X analysers, this is very useful.
Commutability and traceability in EQA programs

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RCPAQAP, St Leonards, Sydney, NSW, Australia

ARTICLE INFO

Keywords: Analytical bias External Quality Assurance Reference material Patient sample commutability Traceability

ABSTRACT

Objectives: The concept of commutability of samples has focused laboratories on the importance of traceability. However, the critical role of External Quality Assurance (EQA) in achieving the primary role of traceability (i.e. facilitating comparable patient results in different laboratories) has largely been lost. The aim of this paper is to review the role of EQA in achieving traceable/commutable results.

Design and methods: The role of commutability and traceability in EQA and Internal Quality Control (IQC) are discussed. Examples of commutable EQA samples are given to highlight the problem of assuming EQA material does not behave like patient samples.

Results: We provide the conventional traceability chain (top down) and the role of EQA in a “bottom up” model using conventional EQA samples.

Conclusions: The quest for commutable samples has compromised the value of EQA without an understanding that some EQA materials are commutable for some measurands.

EQA plays a key role in performance improvement, but laboratories need to understand the importance of using a range of values appropriate to the assay to identify areas of quality need. Traceability and EQA using conventional samples are not mutually exclusive concepts.
FULL TOP DOWN TRACEABILITY

- Primary reference material
- Primary calibrator (assigned value)
- Manufacturer’s master calibrator (assigned value)
- Product calibrator (assigned value)
- Patient sample (result)

- Primary reference method
- Secondary reference method
- Manufacturer’s reference method
- Routine laboratory method
I get the same answer as my Peers.
Proficiency Testing/External Quality Assessment: Current Challenges and Future Directions

W. Greg Miller, 1* Graham R.D. Jones, 2 Gary L. Horowitz, 3 and Cas Weykamp 4

BACKGROUND: Proficiency testing (PT), or external quality assessment (EQA), is intended to verify on a recurring basis that laboratory results conform to expectations for the quality required for patient care.

or harmonization among different measurement procedures.

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The Royal College of Pathologists of Australasia
Quality Assurance Programs
Table 3. Evaluation capabilities of PT/EQA related to scheme design.

<table>
<thead>
<tr>
<th>Category</th>
<th>Commutable</th>
<th>Value assigned with RMP(^a) or CRM</th>
<th>Replicate samples in survey</th>
<th>Absolute vs RMP or CRM</th>
<th>Overall</th>
<th>Peer group</th>
<th>Individual laboratory intralab CV</th>
<th>Measurement procedure interlab CV</th>
<th>Absolute vs RMP or CRM</th>
<th>Relative to participant results</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>X</td>
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</tr>
<tr>
<td>3</td>
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<td>Yes</td>
<td>X</td>
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<td>X</td>
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<td>X</td>
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<tr>
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<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
</tbody>
</table>

\(^a\) RMP, reference measurement procedure; CRM, certified reference material.

\(^b\) Standardization when patient results are equivalent between measurement procedures and calibration is traceable to SI by use of a reference measurement procedure; harmonization when patient results are equivalent between measurement procedures and calibration is not traceable to a reference measurement procedure.
The role of external quality assessment in the verification of in vitro medical diagnostics in the traceability era

Federica Braga*, Sara Pasqualetti, Mauro Panteghini

Research Centre for Metrological Traceability in Laboratory Medicine (CIRM), University of Milan, Milan, Italy

- Quality of the EQA Target
- Commutability of the material
- APS for EQA
EQA Sample Commutability?

- Liquid serum chemistry commutable (but no target assignment);
  - other materials may be single patient,
  - pooled material,
  - correct matrix base (serum, CSF or urine base).

- Other effects are stripping (some), spiking (many), lyophilised (most).

- The QAP are working on assessing the effects of these on commutability.
Due Date: 10/07/2017

Anion Gap (mmol/L)

- Result (\( ^{\circ} \)) for Specimen 5-01 = 19.0 mmol/L
- Result (\( ^{\circ} \)) for Specimen 5-02 = 19.0 mmol/L

Participant No.

Result (\( ^{\circ} \)) for Specimen 5-01 = 19.0 mmol/L
Result (\( ^{\circ} \)) for Specimen 5-02 = 19.0 mmol/L

Current Data for Cycle 5

- Specimen: 5-01, Method: A 21L 069, Median: 17.8, Result: 20.0
- Specimen: 5-02, Median: 16.9, Result: 19.0

SUMMARY DATA

Liquid Serum Chemistry Program

RCPAQAP
The Royal College of Pathologists of Australasia
Quality Assurance Programs
Defining analytical performance specifications: Consensus Statement from the 1st Strategic Conference of the European Federation of Clinical Chemistry and Laboratory Medicine

Model 1: Based on the effect of analytical performance on clinical outcomes
   a. Done by direct outcome studies – investigating the impact of analytical performance of the test on clinical outcomes;
   b. Done by indirect outcome studies – investigating the impact of analytical performance of the test on clinical classifications or decisions and thereby on the probability of patient outcomes, e.g., by simulation or decision analysis.

Model 2: Based on components of biological variation of the measurand.

Model 3: Based on state of the art of the measurement (i.e., the highest level of analytical performance technically achievable).
Opinion Paper


Analytical performance specifications for external quality assessment – definitions and descriptions
Table 2: Example of summary description of analytical performance specifications (APS) based on the RCPAQAP General Serum Chemistry External Quality Assurance (EQA) Scheme.

1. The EQA material is not validated as commutable
2. The overall target-setting method for each measurand is shown below. In addition, method, instrument, reagent manufacturer-based consensus targets are provided based on returned results
3. The APS are to be applied to each individual measurement result
4. The APS are applied for assessment of total error (i.e. the effects of imprecision and bias combined)
5. The rationale for the APS is ‘Aspirational’ (to improve performance) where this is required. The response of the laboratory to ‘out of range’ results should be to review performance and seek improvement
6. The APS are established based on biological variation and state of the art (levels 2 and 3 from Milan conference). The components of biological variation and the level (optimal, desirable, or minimal) are shown below

Further details on the RCPAQAP process used to establish these APS are available [9, 15]

<table>
<thead>
<tr>
<th>Measurand</th>
<th>Assignment of target</th>
<th>Analytical performance specifications</th>
<th>Employed component(s) of biological variation</th>
<th>Quality level</th>
</tr>
</thead>
<tbody>
<tr>
<td>S/P-ALT</td>
<td>IFCC reference procedure in a JCTLM-listed reference laboratory</td>
<td>±5 U/L up to 40 U/L; ±12% &gt;40 U/L</td>
<td>Within-Individual (Imprecision)</td>
<td>Optimal</td>
</tr>
<tr>
<td>S/P-Bicarbonate</td>
<td>Selected well-controlled commercial measuring system by an ISO 15189 accredited clinical laboratories</td>
<td>±2.0 mmol/L up to 20.0 mmol/L; ±10% &gt;20.0 mmol/L</td>
<td>Within- and between-Individual (total error)</td>
<td>Minimal</td>
</tr>
<tr>
<td>S-Transferrin</td>
<td>Median of laboratories participating in EQA</td>
<td>±0.20 g/L up to 2.50 g/L; ±8% &gt;2.50 g/L</td>
<td>Within- and between-Individual (total error)</td>
<td>Minimal</td>
</tr>
</tbody>
</table>
Acceptable Performance Specifications (APS)

• APS based on BV

• Used to allow rapid, standardised assessment of EQA results in both numerical and graphical report formats

• Results outside APS should alert a laboratory that their assay may produce results that are at risk of detrimentally affecting clinical decision making.
Basis

• **Total Error** – Diagnosis
  - Can share reference interval

• **Imprecision** – Monitoring
  - Can monitor patient across laboratories

<table>
<thead>
<tr>
<th></th>
<th>Monitoring ((ALP = 2 \times CV_a))</th>
<th>Diagnosis ((ALP = TE))</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Optimal</strong></td>
<td>(CV_a = \frac{1}{4} CV_i)</td>
<td>(TE = 0.125 \left(CV_i^2 + CV_g^2\right)^{\frac{1}{2}} + 2.33 \times \frac{1}{4} CV_i)</td>
</tr>
<tr>
<td><strong>Desirable</strong></td>
<td>(CV_a = \frac{1}{2} CV_i)</td>
<td>(TE = 0.250 \left(CV_i^2 + CV_g^2\right)^{\frac{1}{2}} + 2.33 \times \frac{1}{2} CV_i)</td>
</tr>
<tr>
<td><strong>Minimal</strong></td>
<td>(CV_a = \frac{3}{4} CV_i)</td>
<td>(TE = 0.375 \left(CV_i^2 + CV_g^2\right)^{\frac{1}{2}} + 2.33 \times \frac{3}{4} CV_i)</td>
</tr>
</tbody>
</table>
**Programs, Analytes and Allowable Limits of Performance**

<table>
<thead>
<tr>
<th><strong>ALCOHOL/AMMONIA</strong></th>
<th><strong>Reviewed January 2012</strong></th>
<th><strong>Basis</strong></th>
<th><strong>Level</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Alcohol</td>
<td>± 2.0 up to 20.0 mmol/L</td>
<td>10% &gt; 20.0 mmol/L</td>
<td>Prof. Opinion</td>
</tr>
<tr>
<td>Ammonia</td>
<td>± 5 up to 50.0 mmol/L</td>
<td>10% &gt; 50.0 mmol/L</td>
<td>Prof. Opinion</td>
</tr>
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</table>

<table>
<thead>
<tr>
<th><strong>ANTIBIOTICS</strong></th>
<th><strong>Reviewed April 2013</strong></th>
<th><strong>Basis</strong></th>
<th><strong>Level</strong></th>
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</thead>
<tbody>
<tr>
<td>Amoxicillin</td>
<td>± 2.0 up to 19.0 mg/L</td>
<td>10% &gt; 19.0 mg/L</td>
<td>Prof. Opinion</td>
</tr>
<tr>
<td>Gentamicin</td>
<td>± 2.0 up to 2.0 mg/L</td>
<td>10% &gt; 2.0 mg/L</td>
<td>Prof. Opinion</td>
</tr>
<tr>
<td>Tobramycin</td>
<td>± 2.0 up to 2.0 mg/L</td>
<td>10% &gt; 2.0 mg/L</td>
<td>Prof. Opinion</td>
</tr>
<tr>
<td>Vancomycin</td>
<td>± 2.0 up to 20.0 mg/L</td>
<td>10% &gt; 20.0 mg/L</td>
<td>Prof. Opinion</td>
</tr>
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</table>

<table>
<thead>
<tr>
<th><strong>BILE ACIDS</strong></th>
<th><strong>Reviewed January 2012</strong></th>
<th><strong>Basis</strong></th>
<th><strong>Level</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Bile Acid</td>
<td>± 4 up to 40.0 mg/dL</td>
<td>10% &gt; 40.0 mg/dL</td>
<td>Prof. Opinion</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>BIODIEGIC ACIDS</strong></th>
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<th><strong>Basis</strong></th>
<th><strong>Level</strong></th>
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<tbody>
<tr>
<td>Adrenaline</td>
<td>± 2.0 up to 100.0 mmol/L</td>
<td>20% &gt; 100.0 mmol/L</td>
<td>Total Error</td>
</tr>
<tr>
<td>Dopamine</td>
<td>± 0.2 up to 2.0 mmol/L</td>
<td>10% &gt; 2.0 mmol/L</td>
<td>Improvement</td>
</tr>
<tr>
<td>ACAA</td>
<td>± 6 up to 40.0 mg/dL</td>
<td>10% &gt; 40.0 mg/dL</td>
<td>Improvement</td>
</tr>
<tr>
<td>20:20:10:80:40:10:60</td>
<td>± 4 up to 20.0 mg/dL</td>
<td>10% &gt; 20.0 mg/dL</td>
<td>Total Error</td>
</tr>
<tr>
<td>HBA</td>
<td>± 6 up to 40.0 mg/dL</td>
<td>10% &gt; 40.0 mg/dL</td>
<td>Improvement</td>
</tr>
<tr>
<td>Metanephrine</td>
<td>± 0.2 up to 2.0 mg/dL</td>
<td>10% &gt; 2.0 mg/dL</td>
<td>Total Error</td>
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<tr>
<td>Noradrenaline</td>
<td>± 0.2 up to 2.0 mg/dL</td>
<td>10% &gt; 2.0 mg/dL</td>
<td>Total Error</td>
</tr>
<tr>
<td>Norepinephrine</td>
<td>± 0.4 up to 2.0 mg/dL</td>
<td>10% &gt; 2.0 mg/dL</td>
<td>Total Error</td>
</tr>
<tr>
<td>3-Methoxytyramine</td>
<td>± 0.2 up to 2.0 mg/dL</td>
<td>10% &gt; 2.0 mg/dL</td>
<td>Total Error</td>
</tr>
<tr>
<td>Serotonin</td>
<td>± 0.2 up to 2.0 mg/dL</td>
<td>10% &gt; 2.0 mg/dL</td>
<td>Total Error</td>
</tr>
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<table>
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<th><strong>BLOOD GASES</strong></th>
<th><strong>Reviewed January 2015</strong></th>
<th><strong>Basis</strong></th>
<th><strong>Level</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Chloride</td>
<td>± 3 up to 100.0 mmol/L</td>
<td>5% &gt; 100.0 mmol/L</td>
<td>Total Error</td>
</tr>
<tr>
<td>Glucose</td>
<td>± 0.4 up to 2.0 mmol/L</td>
<td>10% &gt; 2.0 mmol/L</td>
<td>Improvement</td>
</tr>
<tr>
<td>Phosphate</td>
<td>± 5.0 up to 5.0 mmol/L</td>
<td>10% &gt; 5.0 mmol/L</td>
<td>Improvement</td>
</tr>
<tr>
<td>Lactate</td>
<td>± 0.05 up to 5.0 mmol/L</td>
<td>10% &gt; 5.0 mmol/L</td>
<td>Improvement</td>
</tr>
<tr>
<td>pH</td>
<td>± 0.04</td>
<td></td>
<td>Prof. Opinion</td>
</tr>
<tr>
<td>pCO2</td>
<td>± 2.0 up to 30.0 mg/dL</td>
<td>10% &gt; 30.0 mg/dL</td>
<td>Total Error</td>
</tr>
<tr>
<td>pO2</td>
<td>± 2.0 up to 30.0 mg/dL</td>
<td>10% &gt; 30.0 mg/dL</td>
<td>Total Error</td>
</tr>
<tr>
<td>Potassium</td>
<td>± 0.2 up to 4.0 mmol/L</td>
<td>10% &gt; 4.0 mmol/L</td>
<td>Improvement</td>
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<tr>
<td>Sodium</td>
<td>± 3 up to 150.0 mmol/L</td>
<td>10% &gt; 150.0 mmol/L</td>
<td>Total Error</td>
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<tr>
<td>Urea</td>
<td>± 0.05 up to 6.0 mmol/L</td>
<td>10% &gt; 6.0 mmol/L</td>
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<tr>
<td>Creatinine</td>
<td>± 0.05 up to 100.0 mmol/L</td>
<td>10% &gt; 100.0 mmol/L</td>
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<table>
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<th><strong>CO-OXYGEN</strong></th>
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<th><strong>Basis</strong></th>
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<td>Hemoglobin Concentration</td>
<td>± 6 up to 10.0 g/dL</td>
<td>10% &gt; 10.0 g/dL</td>
<td>Total Error</td>
</tr>
<tr>
<td>Fractional Oxygenhemoglobin</td>
<td>± 5 up to 50.0%</td>
<td>4% &gt; 50.0%</td>
<td>Total Error</td>
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<tr>
<td>Fractional Carboxyhemoglobin</td>
<td>± 1.0 up to 5.0%</td>
<td>20% &gt; 5.0%</td>
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<table>
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<tr>
<td>NT-Pro BNP</td>
<td>± 25 up to 125 ng/L</td>
<td>20% &gt; 125 ng/L</td>
<td>Total Error</td>
</tr>
<tr>
<td>BNP</td>
<td>± 20 up to 100 ng/L</td>
<td>20% &gt; 100 ng/L</td>
<td>Prof. Opinion</td>
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<th><strong>CSF</strong></th>
<th><strong>Reviewed April 2013</strong></th>
<th><strong>Basis</strong></th>
<th><strong>Level</strong></th>
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<td>Albumin</td>
<td>± 0.02 up to 0.1 g/L</td>
<td>20% &gt; 0.1 g/L</td>
<td>Total Error</td>
</tr>
<tr>
<td>Glucose</td>
<td>± 0.2 up to 2.0 mmol/L</td>
<td>10% &gt; 2.0 mmol/L</td>
<td>Total Error</td>
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<tr>
<td>Immunoglobulin G</td>
<td>± 0.02 up to 0.10 g/L</td>
<td>20% &gt; 0.10 g/L</td>
<td>Total Error</td>
</tr>
<tr>
<td>Lactate</td>
<td>± 0.3 up to 2.0 mmol/L</td>
<td>10% &gt; 2.0 mmol/L</td>
<td>Total Error</td>
</tr>
<tr>
<td>Total Protein</td>
<td>± 0.3 up to 0.50 g/L</td>
<td>10% &gt; 0.50 g/L</td>
<td>Total Error</td>
</tr>
<tr>
<td>Bilirubin Concentration</td>
<td>± 0.15 up to 0.60 mmol/L</td>
<td>20% &gt; 0.60 mmol/L</td>
<td>Total Error</td>
</tr>
<tr>
<td>Xanthochromia-Bilirubin screen</td>
<td>± 0.002 up to 0.007 AU</td>
<td>20% &gt; 0.007 AU</td>
<td>Total Error</td>
</tr>
<tr>
<td>Xanthochromia – Haemoglobin screen</td>
<td>± 0.002 up to 0.10 AU</td>
<td>20% &gt; 0.10 AU</td>
<td>Total Error</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>ENDOCRINE</strong></th>
<th><strong>Reviewed January 2012</strong></th>
<th><strong>Basis</strong></th>
<th><strong>Level</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>TSH</td>
<td>± 2.0 up to 2.0 mmol/L</td>
<td>10% &gt; 2.0 mmol/L</td>
<td>Total Error</td>
</tr>
<tr>
<td>T4</td>
<td>± 2.0 up to 100.0 mmol/L</td>
<td>10% &gt; 100.0 mmol/L</td>
<td>Total Error</td>
</tr>
<tr>
<td>T3</td>
<td>± 2.0 up to 100.0 mmol/L</td>
<td>10% &gt; 100.0 mmol/L</td>
<td>Total Error</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>LIPIDS</strong></th>
<th><strong>Reviewed April 2012</strong></th>
<th><strong>Basis</strong></th>
<th><strong>Level</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Cholesterol</td>
<td>± 2.0 up to 2.0 mmol/L</td>
<td>10% &gt; 2.0 mmol/L</td>
<td>Total Error</td>
</tr>
<tr>
<td>HDL Cholesterol</td>
<td>± 0.05 up to 5.0 mmol/L</td>
<td>10% &gt; 5.0 mmol/L</td>
<td>Total Error</td>
</tr>
<tr>
<td>LDL Cholesterol</td>
<td>± 0.05 up to 5.0 mmol/L</td>
<td>10% &gt; 5.0 mmol/L</td>
<td>Total Error</td>
</tr>
<tr>
<td>Triglycerides</td>
<td>± 0.05 up to 5.0 mmol/L</td>
<td>10% &gt; 5.0 mmol/L</td>
<td>Total Error</td>
</tr>
</tbody>
</table>
Target Setting

• The QAP has reference method value assignment for some tests;

• Use of CRMs in field methods for some;

• Weighed in for some;

• "best performing labs" for some;

• Overall median for some (with method specific medians for all).
High order / reference method target setting

ALT, AST, CK, GGT,
LDH
Bilirubin
Glucose
Creatinine

Uric Acid
Sodium
Potassium

Calcium
Magnesium
Lithium
Cortisol
Oestradiol
On the subject of wild mushrooms, it is easy to tell who is an expert and who is not: The expert is the one who is still alive.

— Donal Henahan —
Other issues with Target assignment

- Reference method/SRM availability
- Cost
- Range of concentrations
- Time to get a result
EQALM QUESTIONNAIRE ON TRACEABILITY (2016)

No. of EQA organisations: 58

No. of responders: 14 (= 24%)

No. of responders without CRM / RMP: 6

No. of responders with CRM / RMP: 8 (= 14%)
FRUCTOSAMINE
2. Consensus survey median for each QAP specimen.

GGT
1. IFCC primary reference method.
2. Linear regression of values determined by DGKL Reference Institute for levels 2 to 8 and the DGKL assigned value for level 1.

GLUCOSE
1. Hexokinase or Glucose Oxidase.
2. Linear regression of values determined by WEGAS Reference Laboratory for levels 2 to 8 and the WEGAS assigned value for level 1.

HDL CHOLESTEROL
2. Target set from consensus survey median for levels 1 to 8.

IRON
1. Colorimetric-Ferrozine/Ferene or other colour reagent.
2. Linear regression of data from selected target setting laboratories.

LACTATE
1. Enzymatic, Enzyme Electrode Sensor.
2. Linear regression of data from selected target setting laboratories.

LACTATE DEHYDROGENASE
Three values are provided:
LD (L → P)
1. IFCC reference method.
2. Linear regression of values determined by DGKL Reference Institute for levels 2 to 8 and the DGKL assigned value for level 1.
LD (P → L) - pyruvate>0.7mmol/L
1. Pyruvate Substrate > 0.7 mmolar
2. Consensus survey median for each QAP specimen.
LD (P → L) - pyruvate<0.7mmol/L and Non-rate reactions
1. Pyruvate Substrate < 0.7 mmolar and pyruvate substrates using a non-rate reaction.
2. Consensus survey median for each QAP specimen.

Two values are provided:
Lipase (Reference Range > 300 U/L),
1. Siemens (Dade Behring) users & Ortho Clinical Diagnostics users.
2. Consensus survey median for each QAP specimen
Lipase (Reference Range < 300 U/L)
1. All other methods (excluding above).
2. Consensus survey median for each QAP specimen

LITHIUM
2. Linear regression of values determined by WEGAS Reference Laboratory.

MAGNESIUM
2. Linear regression of values determined by WEGAS Reference Laboratory.

OSMOLALITY
2. Consensus survey median for each QAP specimen.

PHOSPHATE
1. Phosphomolybdate formation and phosphomolybdate reduction.
2. Linear regression of data from selected target setting laboratories.

POTASSIUM
1. Flame Atomic Emission Spectrometry reference method (WEGAS) and Indirect (Diluted) Ion Selective Electrode (selected target setting laboratories).
2. Linear regression of data from selected target setting laboratories.

PROTEIN
1. Biuret - end point with blank or end point no blank.
2. Linear regression of data from selected target setting laboratories.

SODIUM
2. Linear regression of values determined by WEGAS Reference Laboratory.

TIBC
2. Consensus survey median for each QAP specimen.
Despite the availability of a reference measurement system (RMS) for standardizing ALT results in clinical samples, the current evidence is, however, that ALT is still measured by methods that give quite differing values.

Assay performance also varies considerably within users of instruments from the same manufacturer.

This is mainly due to the use on the same platforms of various reagents with different analytical selectivity for ALT.
Figure 2  Steps of the process and different responsibilities for implementing traceability of patient results and defining their uncertainty.
IFCC, International Federation of Clinical Chemistry and Laboratory Medicine; JCTLM, Joint Committee on Traceability in Laboratory Medicine; IQC, Internal Quality Control; EQA, External Quality Assessment.


Editorial

Application of traceability concepts to analytical quality control may reconcile total error with uncertainty of measurement

Mauro Panteghini
### Role of EQA Schemes

- Post market surveillance

---

<table>
<thead>
<tr>
<th>Feature</th>
<th>Aim</th>
</tr>
</thead>
<tbody>
<tr>
<td>EQA material values assigned with reference procedures by an accredited reference (calibration) laboratory</td>
<td>To check the measurement uncertainty of participating laboratories against the reference measurement systems</td>
</tr>
<tr>
<td>Proved commutability of EQA material(s)</td>
<td>To allow transferability of participating laboratory performance to patient samples</td>
</tr>
<tr>
<td>Definition of the clinically allowable uncertainty of measurement</td>
<td>To verify the suitability of laboratory measurements in clinical setting</td>
</tr>
</tbody>
</table>
Standardization in laboratory medicine: Two years’ experience from category 1 EQA programs in Spain

Carmen Ricós1*, Carmen Perich1,2, Beatriz Boned1,3, Elisabet González-Lao1,4, Jorge Díaz-Garzón1,5, Montserrat Ventura6, Sandra Bullich6, Zoraida Cortés1,7, Joana Minchinela1,8, Fernando Marques1,9, Margarita Simón1,10, Virtudes Alvarez1, José-Vicente García-Lario1,11, Pilar Fernández-Fernández1, Pilar Fernández-Calles1,5

1Spanish Society of Laboratory Medicine (SEQCML), Analytical Quality Commission, Barcelona, Spain
2Clinical Laboratory Department, Vall d’Hebron Barcelona Hospital Campus, Barcelona, Spain
3Aragonese Health Service, Royo Villanova Hospital, Zaragoza, Spain
4Quality Healthcare Consulting, ACMS Group, Madrid, Spain
5La Paz University Hospital, Madrid, Spain
6External Quality Assurance Programs, SEQCML, Barcelona, Spain
7Clinical Analysis Service, Hospital San Agustín, Aviles, Principality of Asturias, Spain
8Metropolitan Laboratory (LUMN), Germans Trias i Pujol University Hospital, Badalona, Spain
9Department of Clinical Biochemistry, University Hospital of Salamanca, Salamanca, Spain
10Intercomarcal laboratory consortions of Alt Penedès, Anoia and Garraf, Barcelona, Spain
11Clinical Laboratory, Hospital Campus de la Salud, Granada, Spain

*Corresponding author: cricosaguila@gmail.com
Harmonisation of EQA data

- Common Acceptable Performance Specifications
- Collaboration on newer markers – fewer specialised programs but larger sample sizes
- Sharing of information on poorly performing methods
- Data mining – Reference Intervals, method performance, impact of local standards
Opinion Paper

Gary L. Myers and W. Greg Miller*

The roadmap for harmonization: status of the International Consortium for Harmonization of Clinical Laboratory Results

The International Consortium for Harmonization of Clinical Laboratory Results

OUR VISION

✓ Clinical laboratory test results will be equivalent independent of the clinical laboratory that produced the results

OUR MISSION

✓ To provide a centralized process to organize global efforts to achieve harmonization of clinical laboratory test results
**Key Requirements of an EQA**

- Identify clinical laboratories that are at risk for poor performance
- Assessment of individual method performance
- Characterise test bias and imprecision across multiple methods
- Provide clinical laboratories with reliable information for replacing unsatisfactory methods – post market surveillance
Key Requirements of an EQA

• Assessment of method robustness to clinically relevant interference and quantify their effects across multiple methods

• Satisfy accreditation and Regulatory requirements

• Audit of wider aspects of analytical performance and educational activities.

• Communication with participating laboratories – collect data on broad areas of QA
The future
External Quality Assurance

• Real time

• QC/EQA linked
<table>
<thead>
<tr>
<th></th>
<th>IQC</th>
<th>EQA</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Results</strong></td>
<td>Known</td>
<td>Unknown</td>
</tr>
<tr>
<td><strong>Results Available</strong></td>
<td>Immediately</td>
<td>Later</td>
</tr>
<tr>
<td><strong>Decision purpose</strong></td>
<td>Release or repeat analysis</td>
<td>Quality Improvement</td>
</tr>
<tr>
<td><strong>Frequency</strong></td>
<td>Minimum daily, per batch, per shift</td>
<td>Periodically eg 1 / 4 weeks 2 / 4 weeks 5 x 3 / year</td>
</tr>
<tr>
<td><strong>Concentrations</strong>*</td>
<td>Normal, abnormal</td>
<td>Multiple concentrations, eg 6-8</td>
</tr>
<tr>
<td><strong>Assesses</strong></td>
<td>Bias</td>
<td>Accuracy &amp; imprecision</td>
</tr>
<tr>
<td><strong>Comparison</strong>*</td>
<td>Your lab only</td>
<td>Your lab to all labs &amp; other labs using your method</td>
</tr>
</tbody>
</table>
Results: We observed significant variation and unexpected similarities in practice across laboratories, including QC frequency, cutoffs, number of levels analyzed, and other features.

Conclusions: This variation in practice indicates an opportunity exists to establish an evidence-based approach to QC that can be generalized across institutions.
Patient-Based Real-Time Quality Control: Review and Recommendations

Tony Badrick,1* Andreas Bietenbeck,2 Mark A. Cervinski,3,4 Alex Katayev,5 Huub H. van Rossum,6,7 and Tze Ping Loh,6 on behalf of the International Federation of Clinical Chemistry, and Laboratory Medicine Committee on Analytical Quality
Moving Average for Continuous Quality Control: Time to Move to Implementation in Daily Practice?
Huub H. van Rossum, Hans Kemperman
Clinical Chemistry May 2017, 63 (5) 1041-1043
QC Specimen coming up
Opinion Paper

Tony Badrlick* and Peter Graham

Can a combination of average of normals and “real time” External Quality Assurance replace Internal Quality Control?

https://doi.org/10.1515/cclm-2017-0115
Received February 8, 2017; accepted August 9, 2017

Abstract: Internal Quality Control and External Quality Assurance are separate but related processes that have developed independently in laboratory medicine over but often unrelated activities. IQC has a well-defined statistical basis for the rules to be used; however, the frequency of EQA challenges and determination of allowable limits varies widely across the available programs. Even the aims of different programs are different depending
Frequency of EQA Challenges

- No consensus on frequency
- Regulation driven – minimum
- Should be risk based
- Robustness testing

IF YOU CAN OVERCOME YOUR GREATEST CHALLENGE LIFE WILL BE A PIECE OF CAKE
Tony Badrick*, Stephanie Gay, Mark Mackay and Ken Sikaris

The key incident monitoring and management system – history and role in quality improvement

https://doi.org/10.1515/cclm-2017-0219
Received March 12, 2017; accepted June 29, 2017; previously published online August 3, 2017

Abstract

Background: The determination of reliable, practical Quality Indicators (QIs) from presentation of the patient with a pathology request form through to the clinician receiving the report (the Total Testing Process or TTP) is a key step in identifying areas where improvement is necessary in laboratories.

Methods: The Australasian QIs programme Key Incident
attention and resources on the monitored incident types most important to manage.

Keywords: Failure Mode Effects Analysis (FMEA); post-analytical error; pre-analytical error; Quality Indicators.

Introduction

Clinical laboratories have recognised the importance of pre- and post-analytical errors for some time. For example, a landmark paper from 1997 by Bhaskar and Davenport [1].
### PRE-ANALYTICAL PHASE - COLLECTION AND TRANSPORT INCIDENTS

#### Collection and Transport Samples Rejected - Frequency

<table>
<thead>
<tr>
<th>Sample</th>
<th>Your %</th>
<th>All %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Haem</td>
<td>40.5%</td>
<td>26.7%</td>
</tr>
<tr>
<td>Cb</td>
<td>24.3%</td>
<td>14.6%</td>
</tr>
<tr>
<td>Fill</td>
<td>10.2%</td>
<td>6.6%</td>
</tr>
<tr>
<td>IncSp</td>
<td>5.0%</td>
<td>3.1%</td>
</tr>
<tr>
<td>IncTr</td>
<td>1.5%</td>
<td>0.9%</td>
</tr>
<tr>
<td>Contam</td>
<td>0.3%</td>
<td>0.2%</td>
</tr>
</tbody>
</table>

#### Collection and Transport Samples Rejected - Risk

<table>
<thead>
<tr>
<th>Sample</th>
<th>Your %</th>
<th>All %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Haem</td>
<td>40.5%</td>
<td>26.7%</td>
</tr>
<tr>
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</tr>
<tr>
<td>IncTr</td>
<td>1.5%</td>
<td>0.9%</td>
</tr>
<tr>
<td>Contam</td>
<td>0.3%</td>
<td>0.2%</td>
</tr>
</tbody>
</table>

#### Episodes

- Year: 2017
- All: 61
- Total: 12393771

#### Risk

- Year: 2017
- All: 61
- Total: 2338690

---

#### Collection and Transport (C & T) Incidents

<table>
<thead>
<tr>
<th>Incident</th>
<th>Your Count</th>
<th>All Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sample haemolysed</td>
<td>1024</td>
<td>51134</td>
</tr>
<tr>
<td>Sample clotted</td>
<td>192</td>
<td>14936</td>
</tr>
<tr>
<td>Incorrect fill level of sample</td>
<td>574</td>
<td>5784</td>
</tr>
<tr>
<td>Insufficient sample</td>
<td>151</td>
<td>21923</td>
</tr>
<tr>
<td>Incorrect sample storage or transport</td>
<td>1396</td>
<td>6333</td>
</tr>
<tr>
<td>Sample not collected</td>
<td>1690</td>
<td>35193</td>
</tr>
<tr>
<td>Incorrect sample type</td>
<td>89</td>
<td>9274</td>
</tr>
<tr>
<td>Contaminated sample</td>
<td>16</td>
<td>1164</td>
</tr>
</tbody>
</table>

#### C & T Incidents as % of episodes

- Total C & T Incidents: 5158 / 144791 = 3.56%
- C & T Incidents as % of episodes: 57064 / 1547224 = 3.69%

---

**Key Incident Monitoring & Management Systems**
Laboratory Reliability

• High Risk Results

• Competence assessment process

• QC procedures
Letter to the Editor

Wilson Punyalack, Peter Graham and Tony Badrick*

Finding best practice in internal quality control procedures using external quality assurance performance

https://doi.org/10.1515/cclm-2018-0185
Received February 17, 2018; accepted February 26, 2018

Keywords: best practice in quality control (QC); EQA target setting; survey of QC procedures.

setting’, whereby laboratories with demonstrated ‘good’ performance are invited to assist in determining and confirming the target values for selected measurands. In this letter, we report on the QC practices of those laboratories that are amongst the ‘best’ performers in this EQA program.
IEQA

• Electronic Request and Report

• Analysis of Report data

• Digital Microscopy EQA
A national project for the Standardisation of Pathology Informatics in Australia (SPIA) with support from Government.

Around 80 pathologists, scientists, informaticians, and other clinicians worked in 8 working groups to establish guidelines for the use of terminology and standardised units covering each of the pathology disciplines.
Patient: BLOGGS, Bill  
Date of Birth: 01-Jan-1962  Sex: F  
Patient Location: Hospital Outpatient  

<table>
<thead>
<tr>
<th>Results</th>
<th>Reference</th>
<th>Units</th>
</tr>
</thead>
<tbody>
<tr>
<td>ALP</td>
<td>100</td>
<td>(30-100) U/L</td>
</tr>
<tr>
<td>GGT</td>
<td>95 H</td>
<td>(0-35) U/L</td>
</tr>
<tr>
<td>AST</td>
<td>52 H</td>
<td>(0-30) U/L</td>
</tr>
<tr>
<td>ALT</td>
<td>62 H</td>
<td>(&lt;30) U/L</td>
</tr>
<tr>
<td>Albumin</td>
<td>33 L</td>
<td>(36-52) g/L</td>
</tr>
<tr>
<td>Protein</td>
<td>69</td>
<td>(66-82) g/L</td>
</tr>
<tr>
<td>Bilirubin</td>
<td>7</td>
<td>(&lt;18) umol/L</td>
</tr>
<tr>
<td>Urate</td>
<td>0.31</td>
<td>(0.24-0.42) mmol/L</td>
</tr>
</tbody>
</table>

7.02. Leading zeros required  
7.01. Right alignment of column of results  
7.05. Column of references in brackets  
7.08. Same number of decimals as data  
7.10. Flagged results with H or L to right of result with one space clear.  
7.12. Specimen date as dd-mmm-yy  
7.07. Units column, left justified, to right of reference column  
Formatting of patient name
Summary

- EQA providers have a broader role in post market surveillance - know the limitations of your EQA

- QC has become in many laboratories a poorly understood and practiced process relying on compliance rather than based on risk

- PBRTQC promises better detection of error in real time at low cost – humans shouldn’t make day to day decisions about QC

- There is more we can learn about analytical error by challenging conventional dogma

- We need to be open to change in regard to managing risk and patient safety
a “healthy” cola that aided digestion.

The word ‘Pepsi’ comes from the root word dyspepsia.