Category 5 or 6 EQA programs

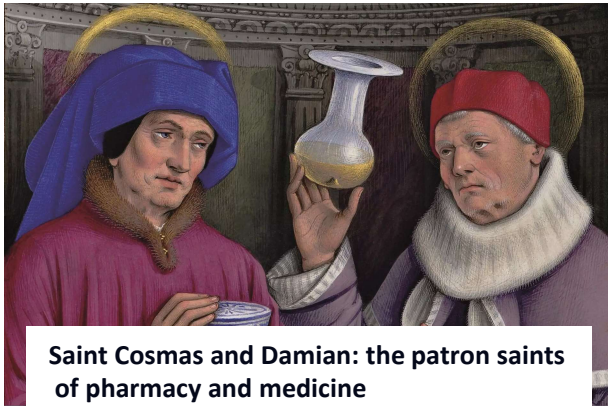
Tony Badrick

October 2022

RCPAQAP
The Royal College of Pathologists of Australasia
Quality Assurance Programs

Approach

1. Category 5 or 6 EQA
2. What is audience for EQA?
3. Where do these programs fit?

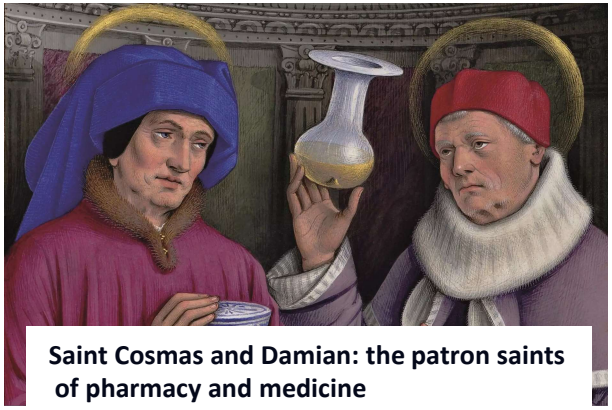


Saint Cosmas and Damian: the patron saints of pharmacy and medicine

RCPAQAP
The Royal College of Pathologists of Australasia
Quality Assurance Programs

Approach

1. Category 5 or 6 EQA
2. What is audience for EQA?
3. Where do these programs fit?



Saint Cosmas and Damian: the patron saints of pharmacy and medicine

RCPAQAP
The Royal College of Pathologists of Australasia
Quality Assurance Programs

Table 3. Evaluation capabilities of PT/EQA related to scheme design.

	Sample characteristics			Evaluation capability						
				Accuracy						
				Individual laboratory					Standardization or harmonization[b]	
					Relative to participant results		Reproducibility		Measurement procedure calibration traceability	
Category	Commutable	Value assigned with RMP[a] or CRM	Replicate samples in survey	Absolute vs RMP or CRM	Overall	Peer group	Individual laboratory intralab CV	Measurement procedure interlab CV	Absolute vs RMP or CRM	Relative to participant results
1	Yes	Yes	Yes	X	X	X	X	X	X	X
2	Yes	Yes	No	X	X	X		X	X	X
3	Yes	No	Yes		X	X	X	X		X
4	Yes	No	No		X	X		X		X
5	No	No	Yes			X	X	X		
6	No	No	No			X		X		

[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.

Clinical Chemistry 57:12
1670–1680 (2011)

Reviews

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.

RCPAQAP
The Royal College of Pathologists of Australasia
Quality Assurance Programs

Category 5 or 6

- Not commutable or verifiably commutable
- No reference value assignment
- May or may not be replicates

RCPAQAP
The Royal College of Pathologists of Australasia
Quality Assurance Programs

Clinical Chemistry 64:3
465–474 (2018)

Special Reports

IFCC Working Group Recommendations for Assessing Commutability Part 3: Using the Calibration Effectiveness of a Reference Material

Jeffrey R. Budd,[1] Cas Weykamp,[2] Robert Rej,[3] Finlay MacKenzie,[4] Ferruccio Ceriotti,[5] Neil Greenberg,[6] Johanna E. Camara,[7] Heinz Schimmel,[8] Hubert W. Vesper,[9] Thomas Keller,[10] Vincent Delatour,[11] Mauro Panteghini,[12] Chris Burns,[13] and W. Greg Miller,[14*] for the IFCC Working Group on Commutability

Clinical Chemistry 59:9
1291–1293 (2013)

Editorials

Commutability Still Matters

W. Greg Miller[1*] and Gary L. Myers[2]

Clinical Chemistry 66:6
749-750 (2020)

Editorial

Further Recommendations on Commutability Assessment

Lindsey G. Mackay*

Clinical Chemistry 64:3
455-464 (2018)

Special Reports

IFCC Working Group Recommendations for Assessing Commutability Part 2: Using the Difference in Bias between a Reference Material and Clinical Samples

Göran Nilsson,[1] Jeffrey R. Budd,[2] Neil Greenberg,[3] Vincent Delatour,[4] Robert Rej,[5] Mauro Panteghini,[6] Ferruccio Ceriotti,[7] Heinz Schimmel,[8] Cas Weykamp,[9] Thomas Keller,[10] Johanna E. Camara,[11] Chris Burns,[12] Hubert W. Vesper,[13] Finlay MacKenzie,[14] and W. Greg Miller,[15*] for the IFCC Working Group on Commutability

Clinical Chemistry 64:3
447–454 (2018)

Special Reports

IFCC Working Group Recommendations for Assessing Commutability Part 1: General Experimental Design

W. Greg Miller,[1*] Heinz Schimmel,[2] Robert Rej,[3] Neil Greenberg,[4] Ferruccio Ceriotti,[5] Chris Burns,[6] Jeffrey R. Budd,[7] Cas Weykamp,[8] Vincent Delatour,[9] Göran Nilsson,[10] Finlay MacKenzie,[11] Mauro Panteghini,[12] Thomas Keller,[13] Johanna E. Camara,[14] Ingrid Zegers,[2] and Hubert W. Vesper,[15] for the IFCC Working Group on Commutability

Clinical Chemistry 66:6
769-778 (2020)

Special Report

IFCC Working Group Recommendations for Correction of Bias Caused by Noncommutability of a Certified Reference Material Used in the Calibration Hierarchy of an End-User Measurement Procedure

W. Greg Miller,[a,*] Jeffrey Budd,[b] Neil Greenberg,[c] Cas Weykamp,[d] Harald Althaus,[e] Heinz Schimmel,[f] Mauro Panteghini,[g] Vincent Delatour,[h] Ferruccio Ceriotti,[i] Thomas Keller,[j] Douglas Hawkins,[k] Chris Burns,[l] Robert Rej,[m] Johanna E. Camara,[n] Finlay MacKenzie,[o] Eline van der Hagen,[d] Hubert Vesper,[p] for the IFCC Working Group on Commutability

Clinical Chemistry 66:2
390-393 (2020)

Letters to the Editor

Beware of Noncommutability of External Quality Assessment Materials for Hemoglobin A_{1c}

fresh whole blood or lyophilized hemolysate samples. A +0.2 mmol/mol bias over 1517 laboratories using fresh whole blood material and a −0.5 mmol/mol bias across 649 laboratories using the lyophilized version of the same pool were used to assess commutability of 23 processed quality-control materials for 17 of the most frequently used HbA_{1c} assays, including immunoassays, enzymatic assays, ion-exchange HPLC, boronate affinity HPLC, and capillary electrophore-

Clinical Chemistry 64:3
421-423 (2018)

Editorials

The Enduring Importance and Challenge of Commutability

Ian S. Young*

Table 1: Characteristics of EQA schemes.

EQA provider	CAP	Noklus[a]	SKML	UK NEQAS
Measurement dates	Nov–Dec 2018	Nov 2018	Oct 2018	Jan 2019
Number of participants	336	75	198	402
Sample characteristics	Frozen pooled serum[b]	Frozen pooled serum[c]	Frozen pooled serum[d]	Frozen pooled serum[e]
Commutability assessment	Previous batch in 2006[f]	Not formally assessed	Previous batch in 2005[d]	Not formally assessed
RMP used	IDMS	IDMS transferred value (see text)	IDMS	IDMS
Creatinine value, µmol/L	61.01	85.00	67.87	70.98
Expanded uncertainty	1.1% (k=2.6)[j]	1.88% (k=2)	1.0% (k=2.6)[j]	0.88% (k=2)

[a]Samples were prepared by the Danish Institute for External Quality Assurance for Laboratories and distributed by Labquality, Finland. [b]Prepared according to Clinical and Laboratory Standards C37 protocol. Samples were stored frozen at –70 °C, distributed on cold packs and thawed in transit. [c]Blood was collected into dry blood bags at Herlev Hospital (Denmark) from seven patients with Hemochromatosis and allowed to clot at 4 °C. Serum was separated on the following day, then frozen at –80 °C in donor bags (approximately 200 mL serum). Frozen serum was stored at –80 °C prior to thawing, pooling, filtration and aliquoting. The aliquots were again stored at –80 °C until shipment on dry ice to Labquality (Finland). The aliquots were thawed and labeled before distributed to participants the same day at ambient temperature. [d]Cobbaert C, Weykamp C, Franck P, de Jonge R, Kuypers A, Steigstra H, et al. Systematic monitoring of standardization and harmonization status with commutable EQA-samples – five year experience from the Netherlands. Clin Chim Acta 2012; 414:234-40 (PMID: 23041212). Samples were stored frozen at –70 °C, distributed on dry ice. [e]Blood was collected into dry blood bags by UK National Blood and Transplant Service at room temperature and allowed to clot at 4 °C. Serum was separated on the following day, then frozen at –40 °C and transferred frozen to UK NEQAS. Frozen serum was stored at –40 °C prior to thawing, pooling, aliquoting and refreezing at UK NEQAS. Specimens were distributed frozen and thawed in transit at ambient temperature. [f]https://www.niddk.nih.gov/health-information/communication-programs/nkdep/laboratory-evaluation/glomerular-filtration-rate/creatinine-standardization/commutability-study. Accessed 20 July 2020. [g]Baadenhuijsen H, Weykamp C, Kuypers A, Franck P, Jansen R, Cobbaert C. Commuteerbaarheid van het huidige monstermateriaal in de SKML-rondzendingen van de algemene klinische chemie. Ned Tijdschr Klin Chem Labgeneesk 2008;33: 154–7. Available translated to English as a supplementary file in Clin Chim Acta 2012;414:234–40. [h]Referenzinstitut fur Bioanalytik, Cologne, Germany. [i]Reference Laboratory WEQAS, Cardiff, UK. [j]K=2.6 from t-distribution for 5 degrees of freedom.

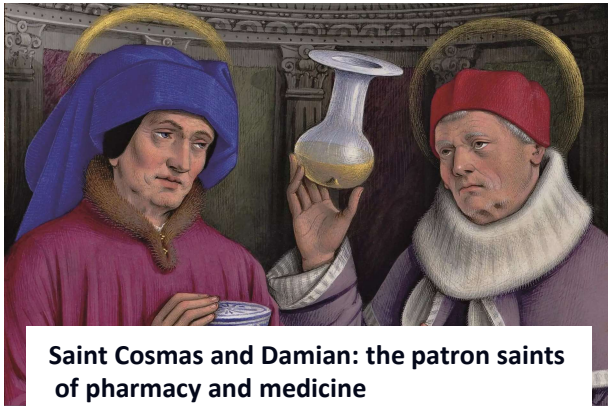
DE GRUYTER Clin Chem Lab Med 2021; 59(1): 117–125

Eline A. E. van der Hagen, Cas Weykamp, Sverre Sandberg, Anne V. Stavelin, Finlay MacKenzie and W. Greg Miller*

Feasibility for aggregation of commutable external quality assessment results to evaluate metrological traceability and agreement among results

Approach

1. Category 5 or 6 EQA
2. What is audience for EQA?
3. Where do these programs fit?



Saint Cosmas and Damian: the patron saints of pharmacy and medicine

RCPAQAP
The Royal College of Pathologists of Australasia
Quality Assurance Programs

Clinical Chemistry 68:4
494-500 (2022)

Q&A

Interpreting EQA—Understanding Why Commutability of Materials Matters

Moderator: Tony Badrick[i,*]
Experts: W. Greg Miller,[a] Mauro Panteghini,[b,c,d] Vincent Delatour,[e] Heidi Berghall,[f] Finlay MacKenzie,[g] and Graham Jones[h]

Opinion Paper

Graham R. D. Jones*, Vincent Delatour and Tony Badrick

Metrological traceability and clinical traceability of laboratory results – the role of commutability in External Quality Assurance

https://doi.org/10.1515/cclm-2022-0038
Received January 14, 2022; accepted February 7, 2022;
published online February 18, 2022

between measurement systems (results harmonization) and demonstration of correct implementation of metrological traceability (methods trueness) become vital, and

EQA Audience – what do they want?

- The laboratory
- Accreditors
- Manufacturers
- Professional or health organisations
- Clinical researchers
- Educators

RCPAQAP
The Royal College of Pathologists of Australasia
Quality Assurance Programs

EQA Audience

- The laboratory
  - Is my laboratory following the manufacturers guidelines for my method?
  - Am I getting the same results as everyone else using this method?
  - Linearity/quality improvement/interference/frequency?
- Accrediting agency
  - Is this laboratory getting the same results as others using this method
  - Good or bad lab?

RCPAQAP
The Royal College of Pathologists of Australasia
Quality Assurance Programs

Clinical Biochemistry 56 (2018) 102–104

Contents lists available at ScienceDirect

Clinical Biochemistry

journal homepage: www.elsevier.com/locate/clinbiochem

Commutability and traceability in EQA programs

Tony Badrick*, Wilson Punyalack, Peter Graham

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.

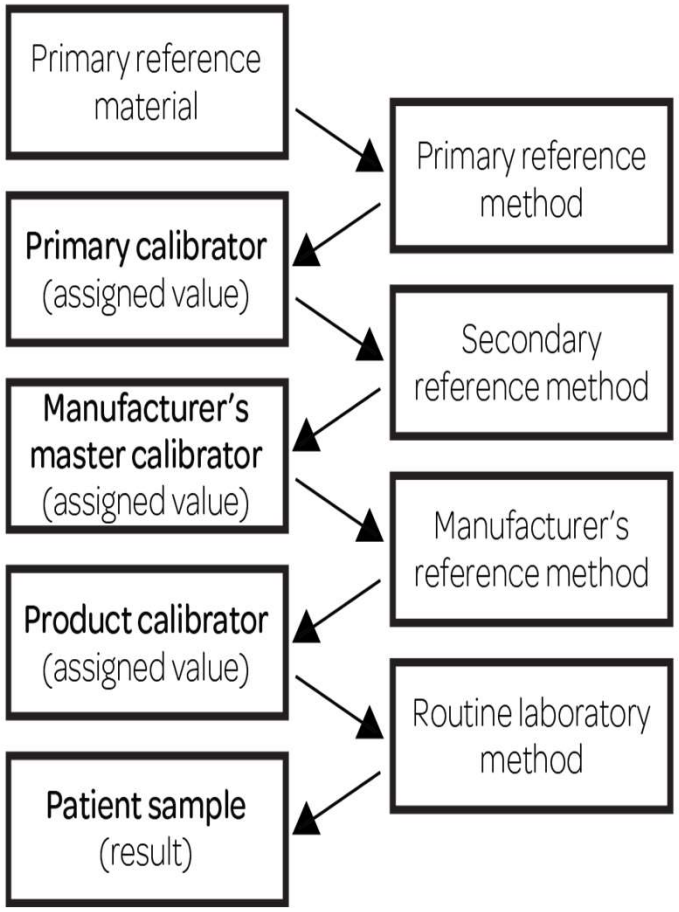
Design and methods: The role of commutability and traceability in EQA and Internal Quality Control (IQC) are discussed. Examples of commutable EQA samples are given to highlight the problem of assuming EQA material does not behave like patient samples.

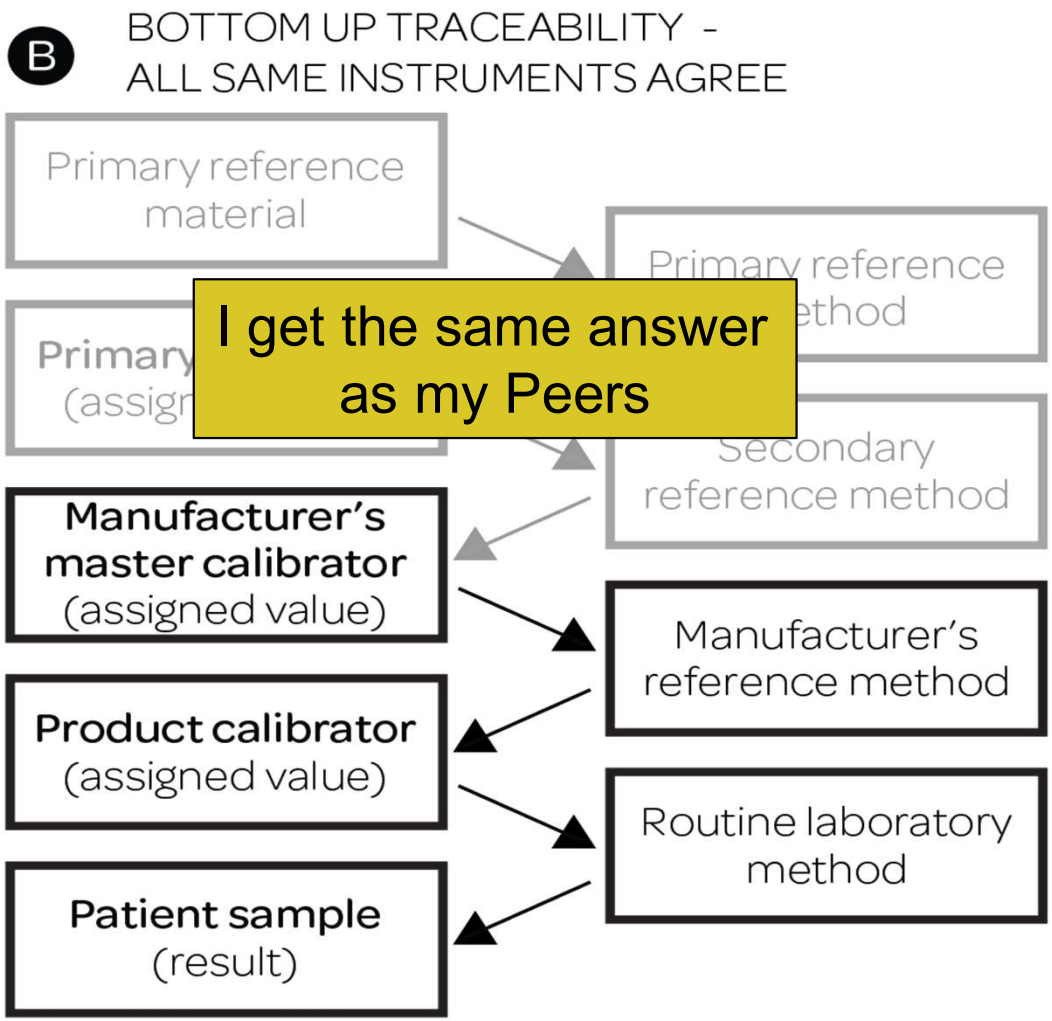
Results: We provide the conventional traceability chain (top down) and the role of EQA in a "bottom up" model using conventional EQA samples.

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.

C FULL TOP DOWN TRACEABILITY





RCPAQAP
The Royal College of Pathologists of Australasia
Quality Assurance Programs

EQA Audience – what do they want?

- Manufacturers
  - Some measurands require traceability, accuracy and comparability of results as a clinical necessity, a regulatory requirement and/or a marketing advantage
  - There are programs specifically aimed at manufacturers and potential customers, such as the CDC Host program for Vitamin D and steroids and the CDC program for lipid.
  - Manufacturers are the organisations that have the power to improve the accuracy of the results from their measurement systems, but this is not an inexpensive exercise, and high-quality data and clinical and business cases need to support these actions.
  - When assay manufacturers take part in standardization programs, accuracy-based programs with commutable materials and reference method value assignment can help them evaluating the effectiveness of the changes in calibration that were made and verify the correct implementation of a new reference measurement system.

EQA Audience – what do they want?

- Professional or health organisations

  - Assess Clinical need/awareness of differences in methods
- common reference intervals
- combining data into clinical databases
- clinical guidelines

- Accuracy based programs can inform decisions about superior methods - creatinine

RCPAQAP
The Royal College of Pathologists of Australasia
Quality Assurance Programs

EQA Audience – what do they want?

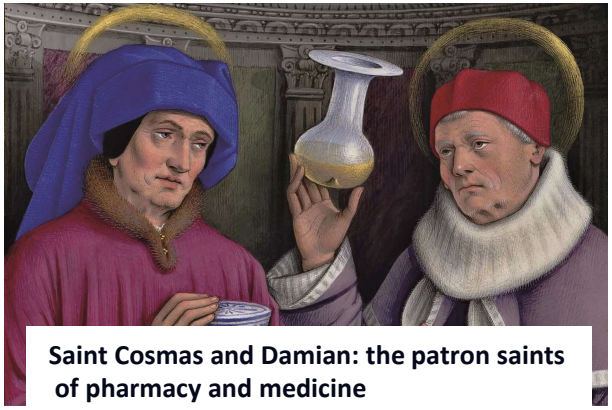
- Clinical researchers
  - Comparing results from one study to another – decision levels

- Educator
  - Training scientists/pathologists
  - Non-commutable material can falsely suggest a method gives misleading information about performance

RCPAQAP
The Royal College of Pathologists of Australasia
Quality Assurance Programs

Approach

1. Category 5 or 6 EQA
2. What is audience for EQA?
3. Where do these programs fit?



Saint Cosmas and Damian: the patron saints of pharmacy and medicine

RCPAQAP
The Royal College of Pathologists of Australasia
Quality Assurance Programs

Risks of using non-commutable EQA

- Changes to calibration over time will not be detected
  - EQA using replicate samples will assist the detection of this drift (time)
  - QC lot – risk
  - Reference Interval?
  - Assessment of lot-lot change – Patient-Based QC

- Lack of comparability of results from other methods – patient risk

- Relies on manufacturer providing traceability - clinical decision points

RCPAQAP
The Royal College of Pathologists of Australasia
Quality Assurance Programs

Category 5 or 6 – what is lost

- Not commutable or verifiably commutable
  - Changes in EQA(QC) may not reflect patient values
  - Cant compare with other methods

- No reference value assignment
  - What is true value?

- May or may not be replicates
  - Lot-lot/calibration changes – QC for QC!

RCPAQAP
The Royal College of Pathologists of Australasia
Quality Assurance Programs

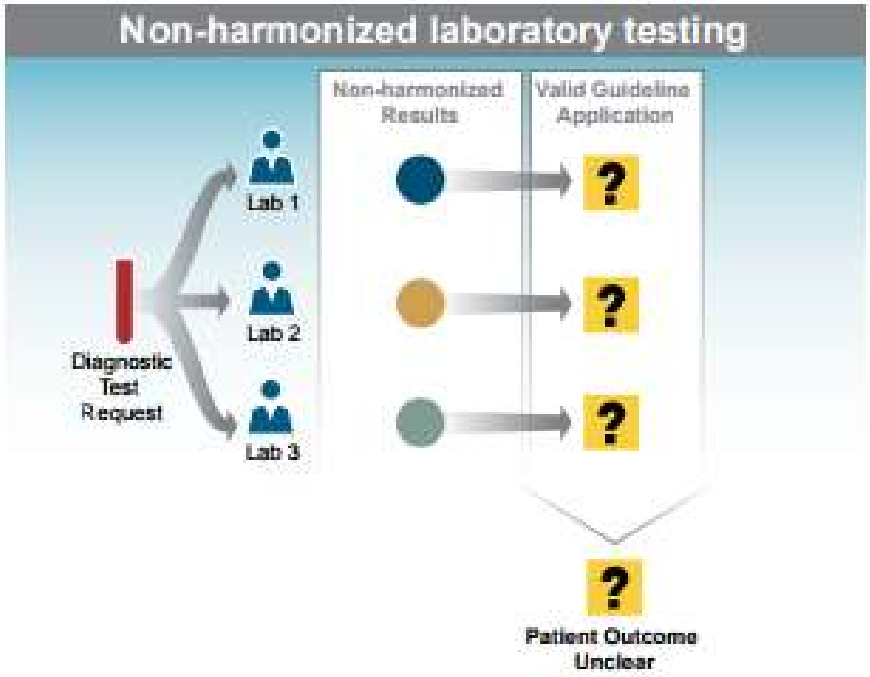
Category 5 or 6 – the value

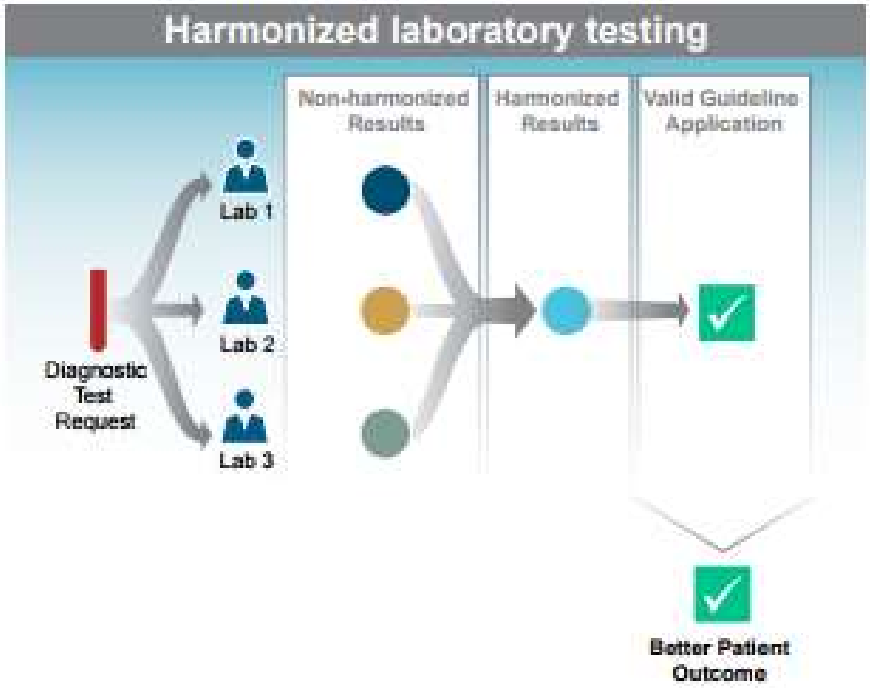
- Not commutable or verifiably commutable
  - Cost of verifying commutability
  - Volumes required for EQA
  - Stability of material

- No reference value assignment
  - cost

- May or may not be replicates

RCPAQAP
The Royal College of Pathologists of Australasia
Quality Assurance Programs





AACC Better health through laboratory medicine.

What are

COMMUNITY | SCIENCE & RESEARCH | CLINICAL LABORATORY NEWS | EDUCATION | MEETINGS

AACC.org // Advocacy & Outreach // Advocacy Priorities // Improving Patient Care Through Harmonized Test Results

Improving Patient Care Through Harmonized Test Results

RCPAQAP
The Royal College of Pathologists of Australasia
Quality Assurance Programs

EQA

QC

measurement procedure (ms.)

material (m.)

ms. 1
Fit for purpose measurement procedure(s) for purity assessment of identity assessment or identity off pure substances, e.g. qNMR, mass balance, gene sequencing

ms. 2
Primary reference measurement procedure for calibrator. Weighing of the certified primary reference material m. 1

ms. 3
Reference measurement procedure for the measurand. conforming to ISO 15193

ms. 4
Manufacturers selected measurement procedure

ms. 5
Manufacturers standing measurement procedure

ms. 6
End-users in vitro diagnostic measurement device

m. 7
Synthetic QC sample

m. 1
Certified primary reference material - ISO 15194 conforming

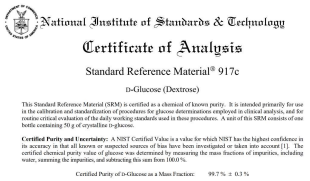
m. 2
Primary calibrator - prepared as solution of m. 1 in suitable solvent

m. 3
Secondary, commutable certified reference material conforming to ISO 15193. Matrix is pooled human plasma

m. 4
Manufacturers working calibrator

m. 5
Calibrator for the end-user measurement device

m. 6
Human sample with result


National Institute of Standards & Technology

Certificate of Analysis

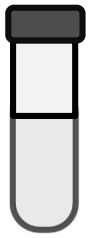
Standard Reference Material® 917c

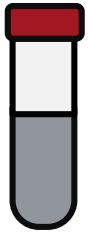
D-Glucose (Dextrose)

This Standard Reference Material (SRM) is certified as a chemical of known purity. It is intended primarily for use in the calibration and standardization of procedures for glucose determinations employed in clinical analysis, and for routine critical evaluation of the daily working standards used in those procedures. A unit of this SRM consists of one bottle containing 50 g of crystalline D-glucose.

Certified Purity and Uncertainty: A NIST Certified Value is a value for which NIST has the highest confidence in its accuracy in that all known or suspected sources of bias have been investigated or taken into account [1]. The certified chemical purity value of glucose was determined by measuring the mass fractions of impurities, including water, summing the impurities, and subtracting this sum from 100.0 %.

Certified Purity of D-Glucose as a Mass Fraction: 99.7 % ± 0.3 %





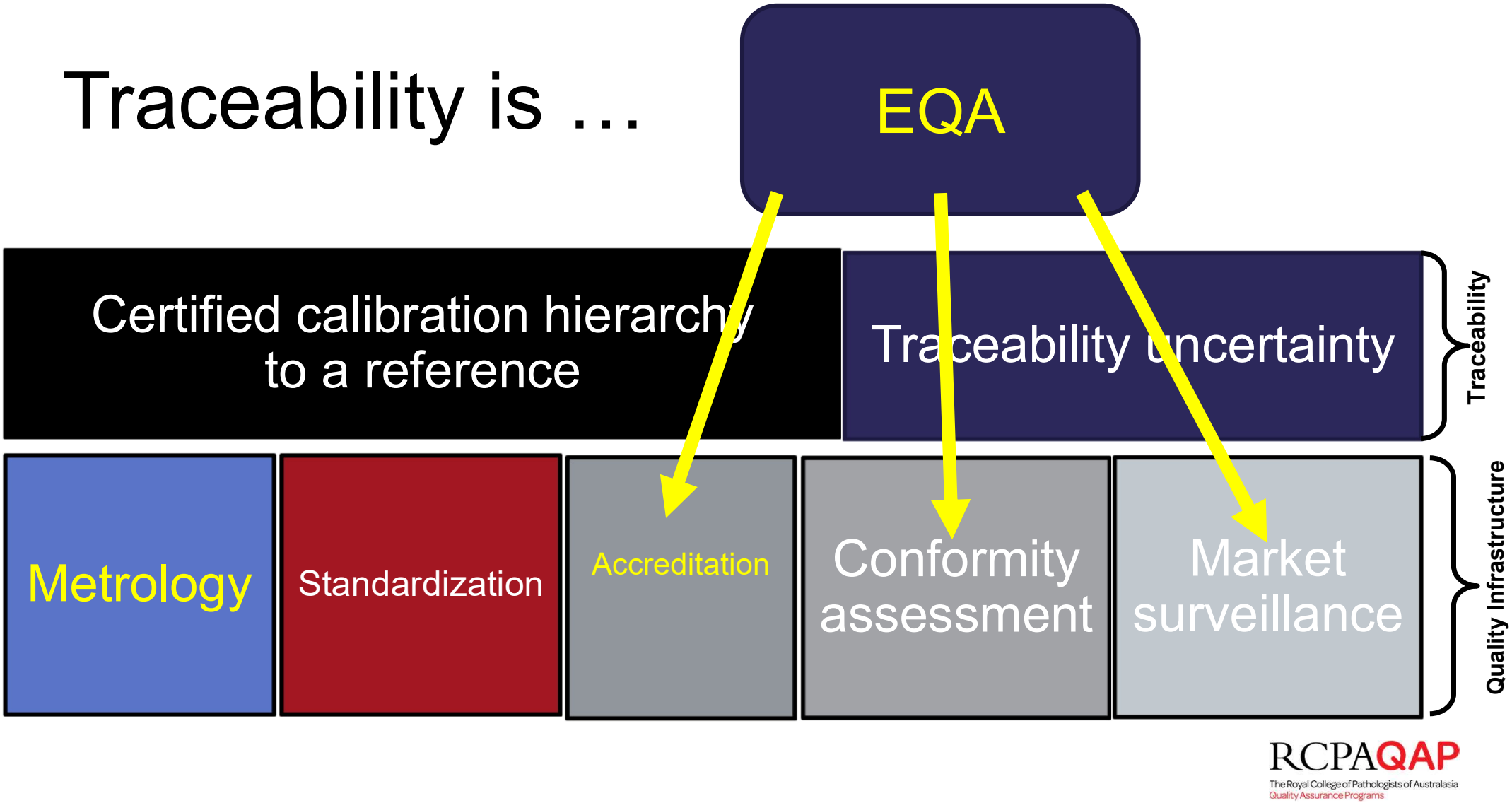
Metrology Institute

Manufacturer

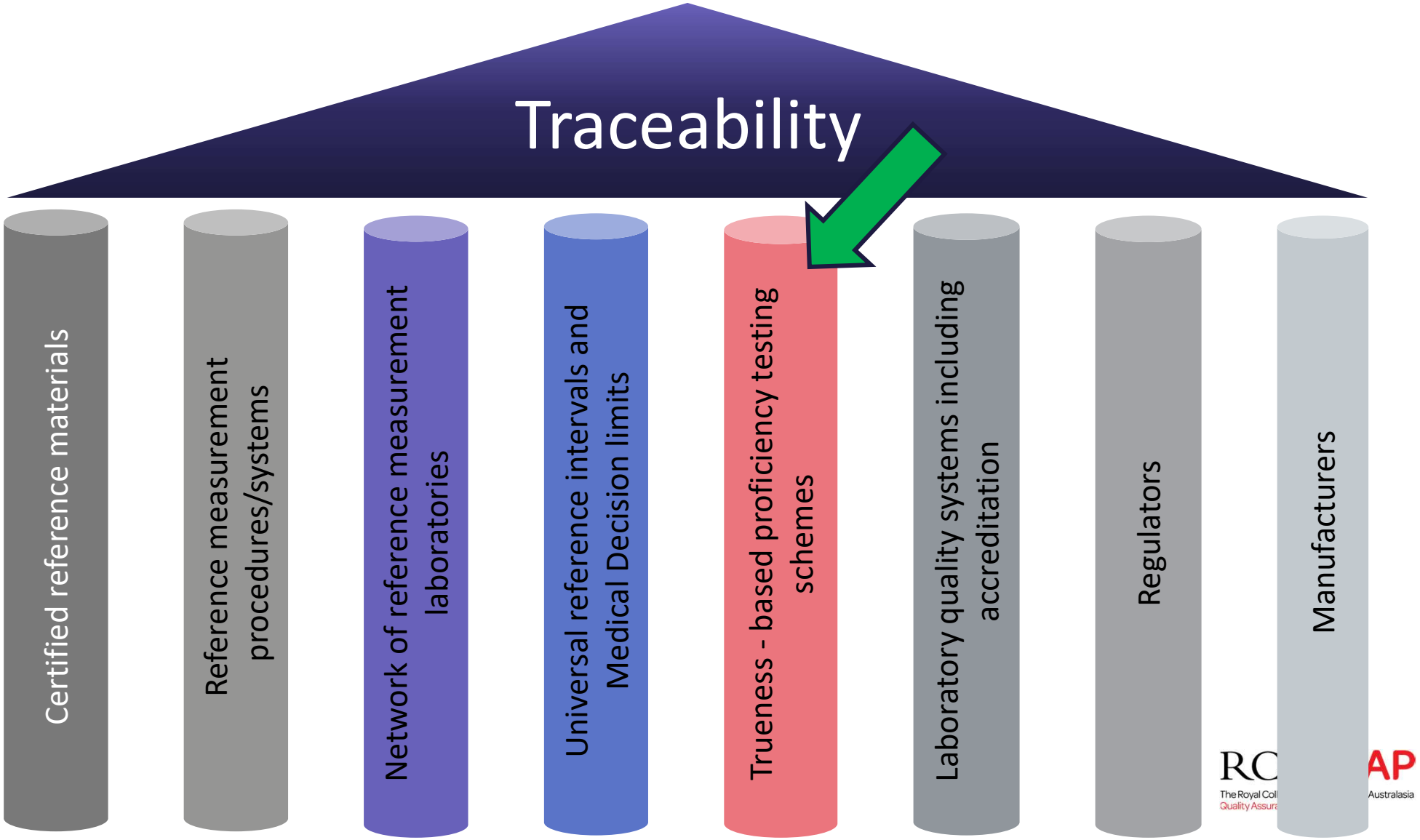
End users

RCPAQAP
The Royal College of Pathologists of Australasia
Quality Assurance Programs

Traceability is …



RCPAQAP
The Royal College of Pathologists of Australasia
Quality Assurance Programs


Traceability
Certified reference materials
Reference measurement procedures/systems
Network of reference measurement laboratories
Universal reference intervals and Medical Decision limits
Trueness - based proficiency testing schemes
Laboratory quality systems including accreditation
Regulators
Manufacturers

Bureau International des Poids et Mesures

Database of higher-order reference materials, measurement methods/procedures and services

JCTLM Accurate results for patient care

> You are here : JCTLM-DB

JCTLM database: Laboratory medicine and *in vitro* diagnostics

JCTLM Newsletters
- Issue 9 - April 2022
- Previous Issues

JCTLM Database
- Search Form
- List of reference materials no longer listed in the JCTLM Database
- List of reference measurement methods no longer listed in the JCTLM database
- Contact us
- Survey Form

JCTLM
- *Preamble*
- Joint Committee for Traceability in Laboratory Medicine (JCTLM)

Analyte keyword search for reference materials, measurement methods/procedures and services

Type an analyte name in part or full, e.g. cholesterol

Refine search by analyte category All

Refine search by matrix category All

Please select your requirement :
- (•) Higher-order reference materials
- ( ) Reference measurement methods/procedures
- ( ) Reference measurement services

Reset Search

Download entries as PDF

Please select your requirement :
- ( ) Higher-order reference materials
- ( ) Reference measurement methods/procedures
- ( ) Reference measurement services

Select an analyte category Download

Select a matrix category Download

View a list of all entries Download

Printable version Back to top

JCTLM

List of available certified reference materials for Metabolites and substrates

PDF description of material contains limited information on materials. More complete information can be retrieved from the keyword search results for the reference materials (http://www.bipm.org/jctlm/).

The (Certified) Reference Materials listed in the JCTLM database have been reviewed for compliance with ISO 15194:2009 unless otherwise stated.

The higher-order reference materials listed below are categorized in three lists:

List I: Certified reference materials and reference measurement methods/procedures for well-defined chemical entities or internationally recognized reference method-defined measurands.
Reference materials and measurement methods/procedures included in this category are those that provide values that are traceable to the SI units; e.g., electrolytes, enzymes, drugs, metabolites and substrates, non-peptide hormones, and some proteins.

List II: Reference materials for which values of the measurands are not SI-traceable but are assigned by or traceable to an internationally agreed upon protocol, e.g., reference materials for blood typing, coagulation factors, microbial serology, nucleic acids, and some proteins.
List II also contains a group of purified substances which, due to the absence of reference measurement procedures, should not be directly used for calibration of routine methods unless commutability is established and/or matrix effect independent internationally recognized standardized value transfer protocols to commutable samples are applied.

List III: Certified Reference Materials for nominal properties.

Analyte	Matrix/Material	Name of the reference material	Producer	Quantity	Range of certified values in reference material	Range of expanded uncertainties for certified value	Listed in
alanine	0.1 mol/L hydrochloric acid	SRM 2389a, Amino Acids in 0.1 mol/L Hydrochloric Acid	NIST (National Institute of Standards and Technology), United States Phone : +1 301 975 6776 Fax : +1 301 948 3730 srminfo@nist.gov	Mass fraction	0.223 mg/g	0.007 mg/g Level of confidence 95 %	List I

Greyed out rows indicate the (Certified) Reference Materials reviewed for compliance with ISO 15194:2003 but not reviewed against ISO 15194:2009.

RCPAQAP
The Royal College of Pathologists of Australasia
Quality Assurance Programs

Our Responsibility

- Demonstrate the value of commutable EQA to labs and health professionals

- Most labs are not aware of this!

- QAP Audit (Cat 4 and 5 EQA)
  - Which methods can share reference intervals
  - Which methods can be combined in an EHR

RCPAQAP
The Royal College of Pathologists of Australasia
Quality Assurance Programs

Summary

- Category 5 or 6 are not commutative or have reference value assignment
- To achieve category 1 or 2 is expensive and perhaps prohibitive
- Labs need to understand the limitations of different materials used in EQA programs
- EQA providers need to meet the challenge now before us!

RCPAQAP
The Royal College of Pathologists of Australasia
Quality Assurance Programs