St Vincent's Hospital
A facility of St Vincents & Mater Health Sydney

SYDPATH
ST VINCENT'S PATHOLOGY

Why Traceability Matters to Patients?

(and you are all patients)

Graham Jones
Department of Chemical Pathology
St Vincent's Hospital, Sydney

JCTLM Members and Stakeholders meeting, Paris 2017

JCTLM
Accurate results for patient care

Acknowledgements

Organisations are vital for advances

Contents

- **Why traceability is important to the public**
  (a talk-within-a-talk where we pretend you are not experts)

- **What else is needed to benefit from traceable results?**
  - **Terminology**
  - **EQA**
  - **Reference Intervals**
  - **Knowing if a result is traceable**

St Vincent's Hospital
A facility of St Vincents & Mater Health Sydney

SYDPATH
ST VINCENT'S PATHOLOGY

Why Traceability Matters to Patients?

Graham Jones
Department of Chemical Pathology
St Vincent's Hospital, Sydney

Interested Members of the Public

Paris 2017

JCTLM
Accurate results for patient care

St Vincent's Hospital
A facility of St Vincents & Mater Health Sydney

SYDPATH
ST VINCENT'S PATHOLOGY

Why Metrological Traceability of Pathology Results Matters to Patients?

Graham Jones
Department of Chemical Pathology
St Vincent's Hospital, Sydney

Interested Members of the Public

Paris 2017

JCTLM
Accurate results for patient care

Presentation Contents

- What is traceability?
- History of traceability
- Why is it important for laboratory medicine
- What we need to do

What is traceability?

What is traceability?

- Traceability is how we get the right result

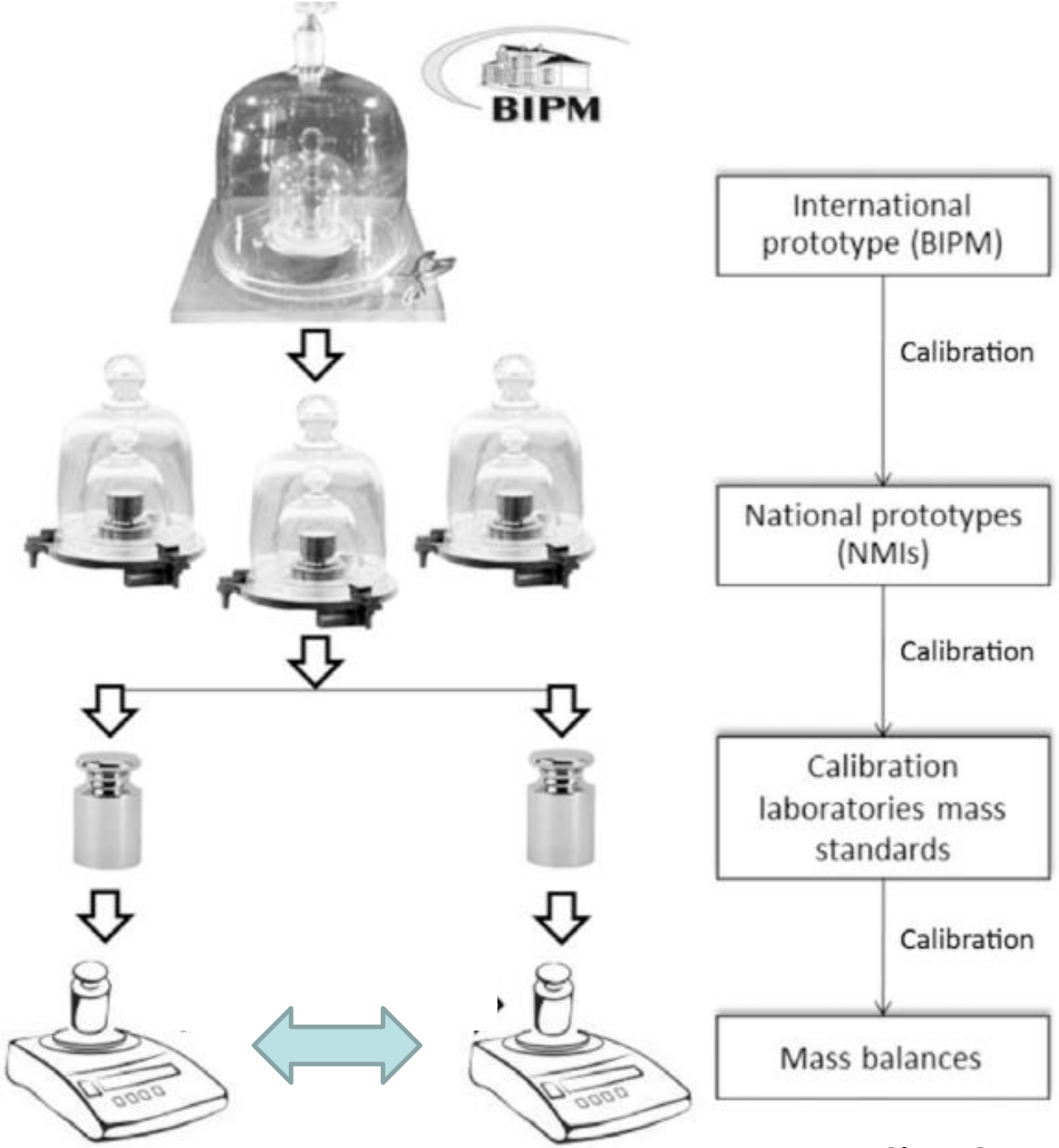
What is the right result?

- An accurate result
- The result we would get with the best method in the best lab

How does traceability work?

- Behind the scenes our results have been made to be the same as those from the best methods
- More later…

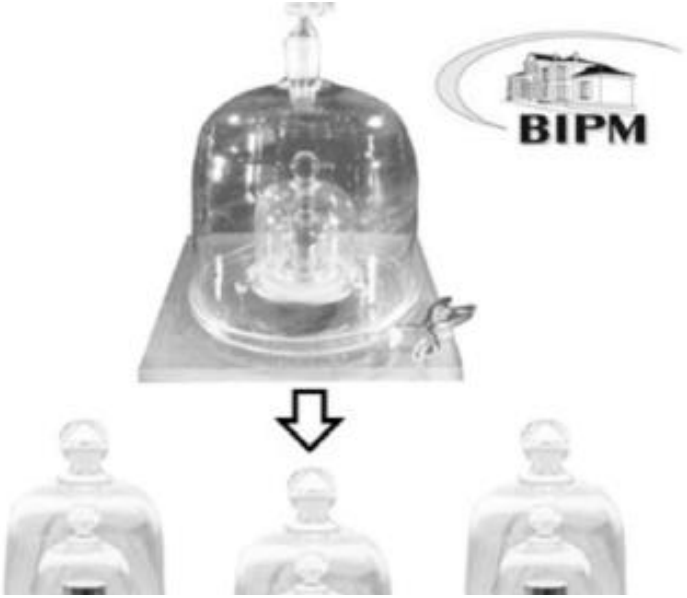
“The Kilo”
BIPM, Paris

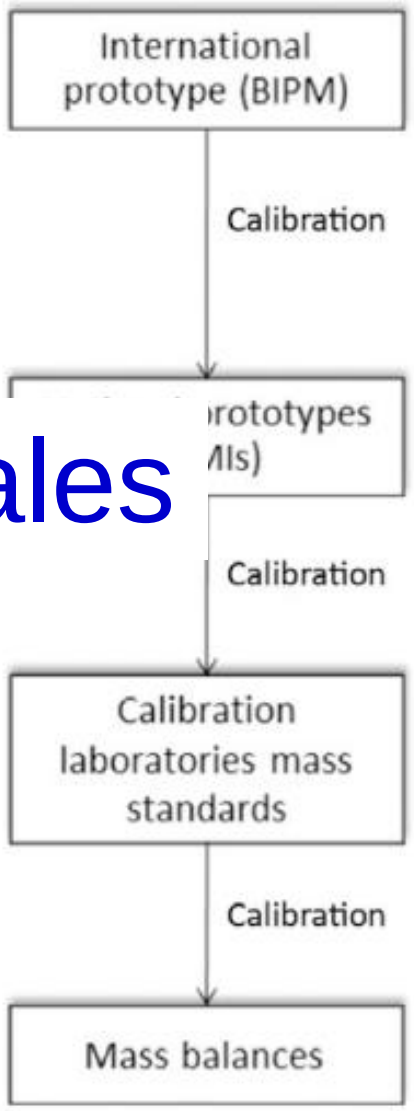


Traceable results are comparable

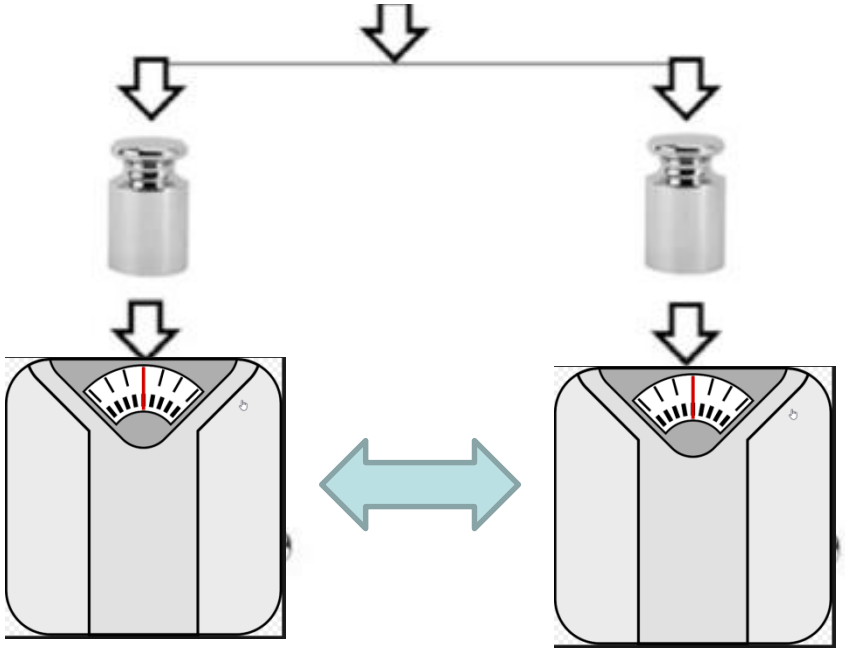
J. Braz. Chem. Soc. vol.26 no.2
São Paulo Feb. 2015

“The Kilo”
BIPM, Paris





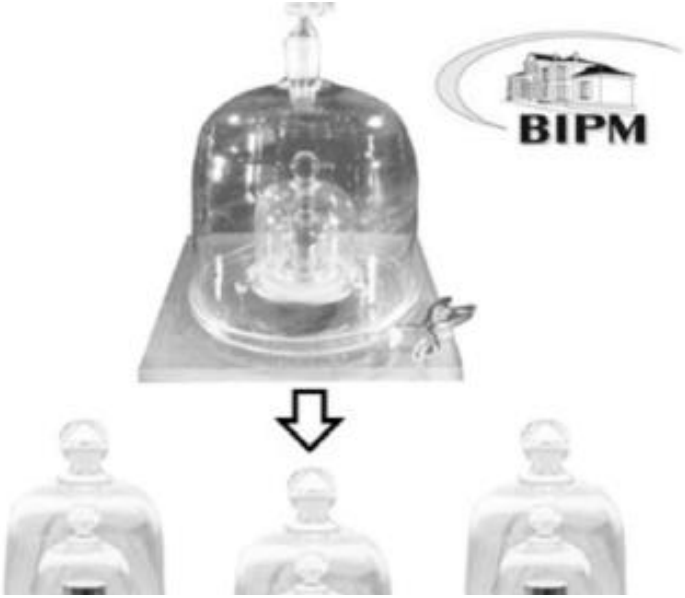
Same for Bathroom scales



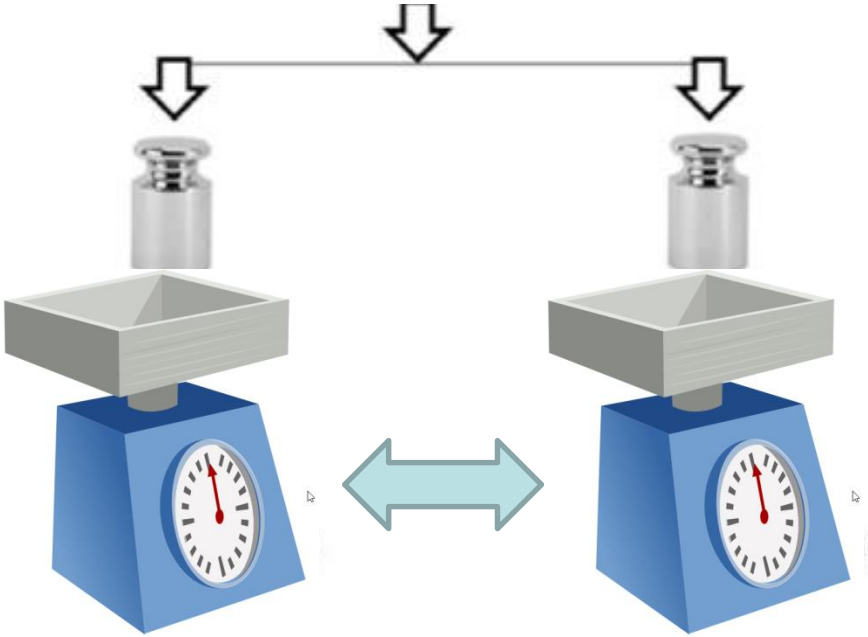
Traceable results are comparable

J. Braz. Chem. Soc. vol.26 no.2
São Paulo Feb. 2015

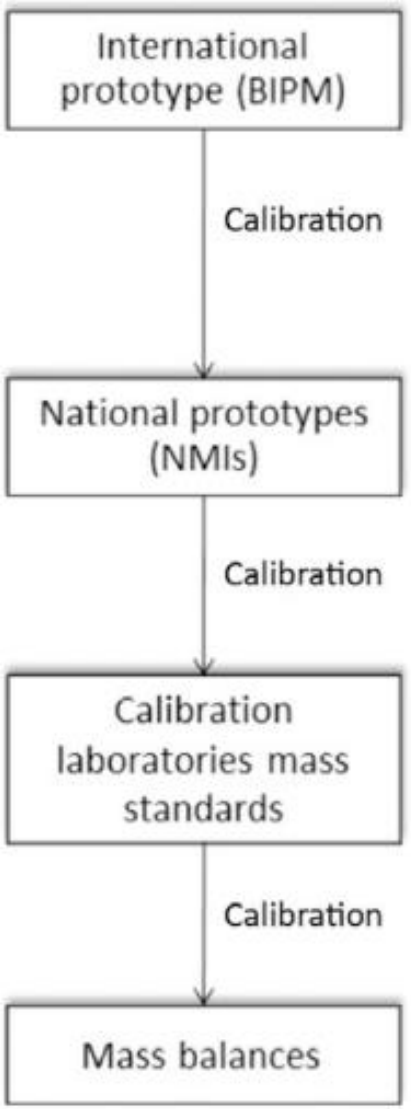
“The Kilo”
BIPM, Paris



And for kitchen scales



Traceable results are comparable



J. Braz. Chem. Soc. vol.26 no.2
São Paulo Feb. 2015

Traceable Measurements

- Weight (mass)
- Length
- Time
- Temperature

…….

We take it for granted that these measurement are comparable

Metrology - BIPM

Bureau International de Poids et Mesures
(International Bureau of Weights and Measures)

(Pont de Sevres, Paris)

Systeme Internationale

Base quantity	SI base unit	
Name	Name	Symbol
length	metre	m
mass	kilogram	kg
time, duration	second	s
electric current	ampere	A
thermodynamic temperat	kelvin	K
amount of substance	mole	mol
luminous intensity	candela	cd

Systeme Internationale

Base quantity	SI base unit	
Na		
len		
ma		
tim		
ele		
the		
am		
luminous intensity	candela	cd

For Users of Imperial Units

The ounce, pound, stone, ton, inch, foot, mile (etc), are all traceable to SI (using conversion factors)

Traceability - Terminology

- **Measurement** Traceability
- Trueness
- Bias
- Accuracy
- Comparability
- Equivalence
- “Getting the right answer”

- **Traceability makes results the same: anywhere, any time**

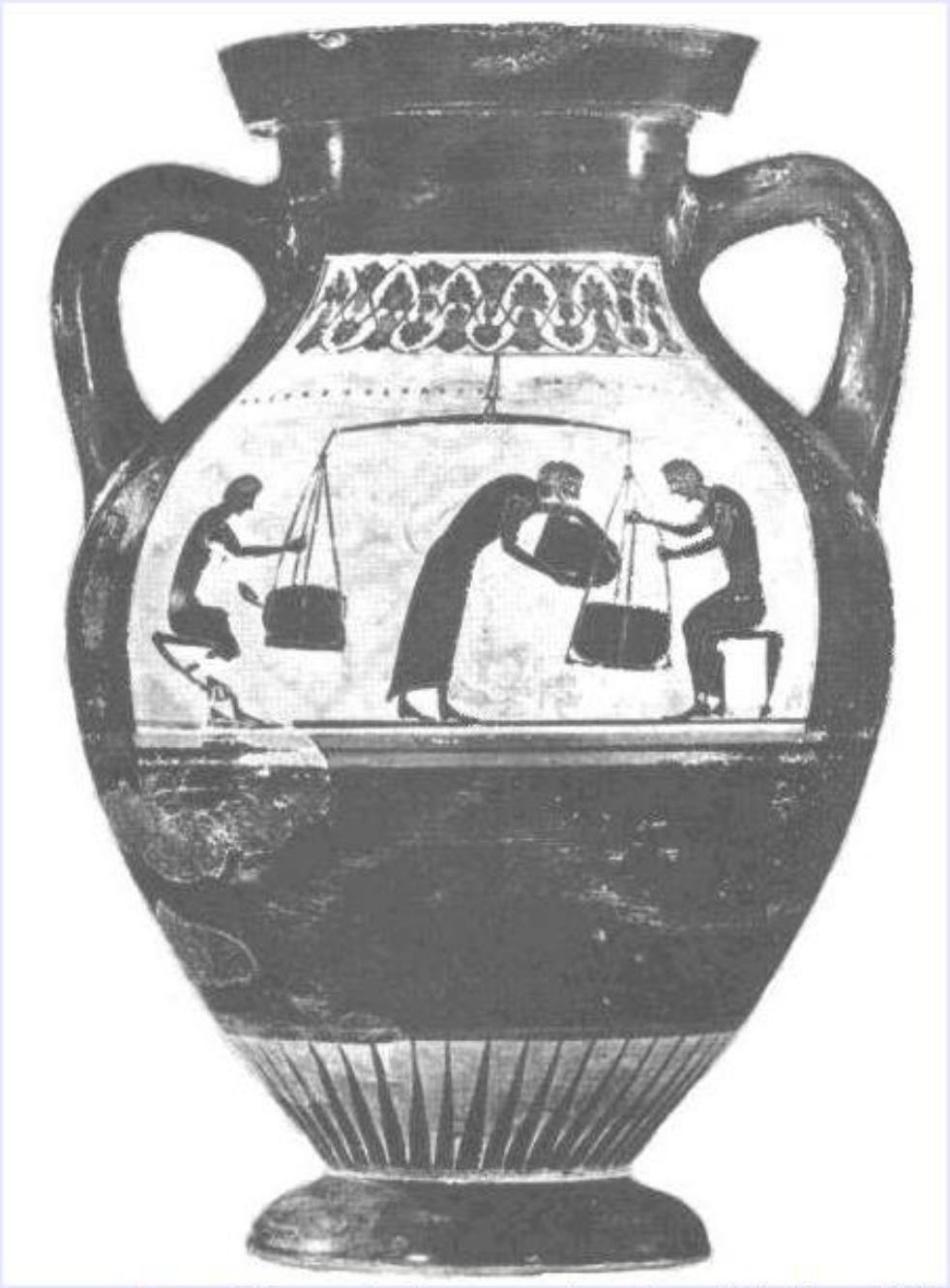
Modern Measurements

Our current scientific, manufacturing, trade and technological civilization is built on traceable measurements – The Systeme Internationale (SI)

Measurements in History

- Egyptian Engraving ~1600 BC

Balances used to measure by comparison



Black figure amphora. Men weighing merchandise, Taleides 560 - 530 BC

Mass – Ancient Greece

- Set of official weights, about 500 B.C.
- Found near the Tholos
- Inscribed with the name of the weight and a symbol.
- Also inscribed with the phrase *demosion Athenaion,* "public (property) of the Athenians."

Length (cubit)

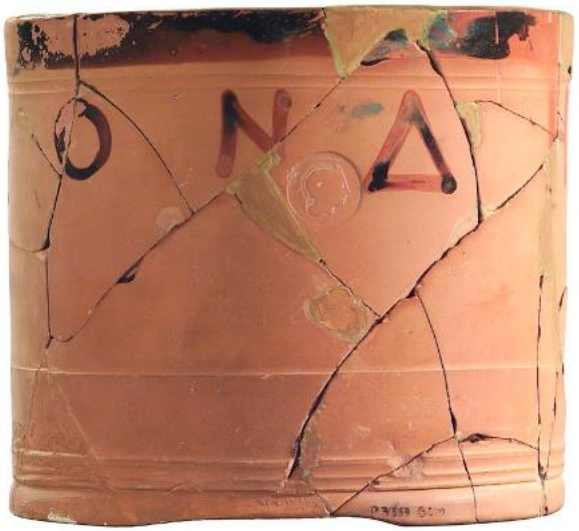
Cubit rod of Maya (1300 BC)

1.1% difference

Fourteen cubit rods range from 523.5 to 529.2 mm and are divided into seven palms, each palm is divided into four finger and the fingers are further subdivided.

Volume

- Clay public measure
- 4th century B.C.
- Inscribed *demosion,* indicating that it is official.
- Validating stamps are included.



Chia Measure: China 45 BC – AD 23

國立故宮博物院
NATIONAL PALACE MUSEUM

Taiwan

Combination of five volume measures.

2 he = 1 ho, 10 ho = 1 sheng, 10 sheng = 1 tou, 10 tou = 1 hu.

Inscription of 249 characters explains the origins, individual parts, and dimensions of the individual parts.

Measurements

By about 500 BC, Athens had a central depository of official weights and measures, the Tholos, where merchants were required to test their measuring devices against official standards.

By about 1875 AD, The modern world had a central depository of official weights and measures, the BIPM, where measurement services were required to test their measuring devices against official standards.

BIPM

What do you want from your lab?

An accurate Result!
(a traceable result)

what does this mean?

Numerical laboratory results

Example:

Mr Bill Bloggs (DoB 1 Jul 1950)

Sample Collected: 21 Aug 2012, 10:00 am

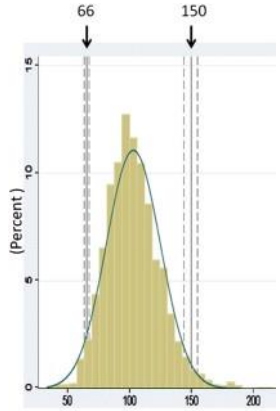
Test	Result	Units
Serum creatinine:	**125**	umol/L

Interpreting laboratory results

Interpreting laboratory results

Your results are interpreted by comparison with:

- **A clinical decision point**
- **A reference interval (normal range)**



- **Your previous result**

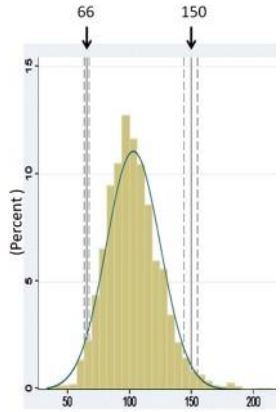
	5-Aug	1-Aug	
Creatinine:	**110**	**125**	umol/L

Professor Per-Hyltoft Peteresen, Sydney 2005

Interpreting laboratory results

Your results are *correctly interpreted* when your *lab result* is comparable to:

- **A clinical decision point**
  - ***The method used in the paper***
- **A reference interval (normal range)**
  - ***The method used in the study***
- **Your previous result**
  - ***The method used for previous result***



	5-Aug	1-Aug	
Creatinine:	**110**	**125**	umol/L

Professor Per-Hyltoft Peteresen, Sydney 2005

Does it matter if results are different?

Applying Evidence

When comparing with a clinical decision point derived from the medical literature

- **You want the best evidence**
- **Medical evidence comes from everywhere in the world**
- (Freely available: INTERNET!)

- ***Labs around the world must be traceable to allow "Evidence-based medicine"***

E-Health

- The Future is an **Electronic Medical Record**
- Patients want “all pathology results available”
- Different labs need to be comparable
  (or display and interpretation difficult)
- The public expects this!

→ Labs must be traceable to be IT Ready

When patients travel…

- From GP to hospital
- From GP to specialist
- Use a different laboratory
- To a different city
- To a different country (holiday, work, migration)

- To manage your health, you need your pathology results from different labs need to be the same

All labs must be traceable to allow you to move

Financial effects?

- When results are not comparable
- Patients need to be tested again when:
  - Admitted to hospital
  - Visiting specialist
  - Changing location or laboratory

→ Traceable results avoid Waste

Big Data / Data Mining

- Involves combining data from many sources
- Used to see patterns, plan services
- Requires comparable results

Traceable results are needed for combining databases

If the laboratories are different:

Results not comparable with other lab: (biased) →

- Wrong diagnosis
- Wrong management
- Incorrect monitoring

→ Traceable results can avoid patient harm

Public expectations

- “you are scientists aren’t you”
- “why are the results different in different labs”

- Because commutable, historical, new method, blah, blah blah ….

Traceable results are what the public expects

Without comparable results ..

Laboratory Medicine is:

Not evidence-based

Not IT Ready

Not safe

Wasteful

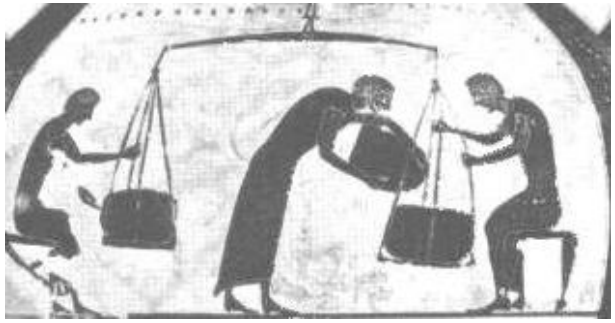
Doesn't serve patients needs

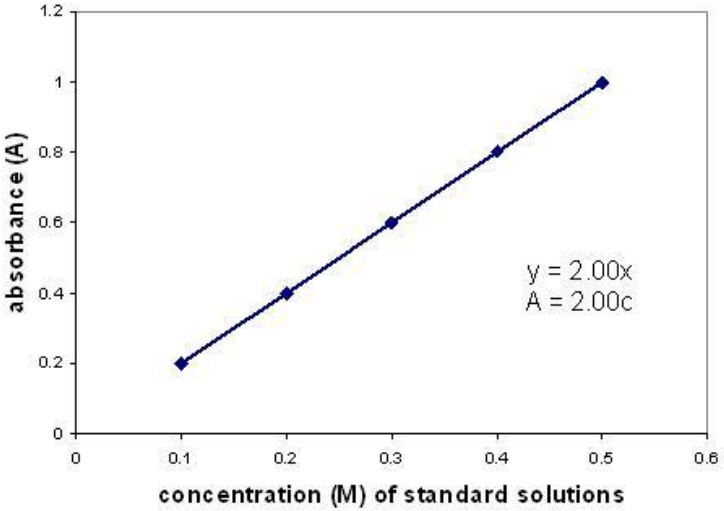
You need traceable results!

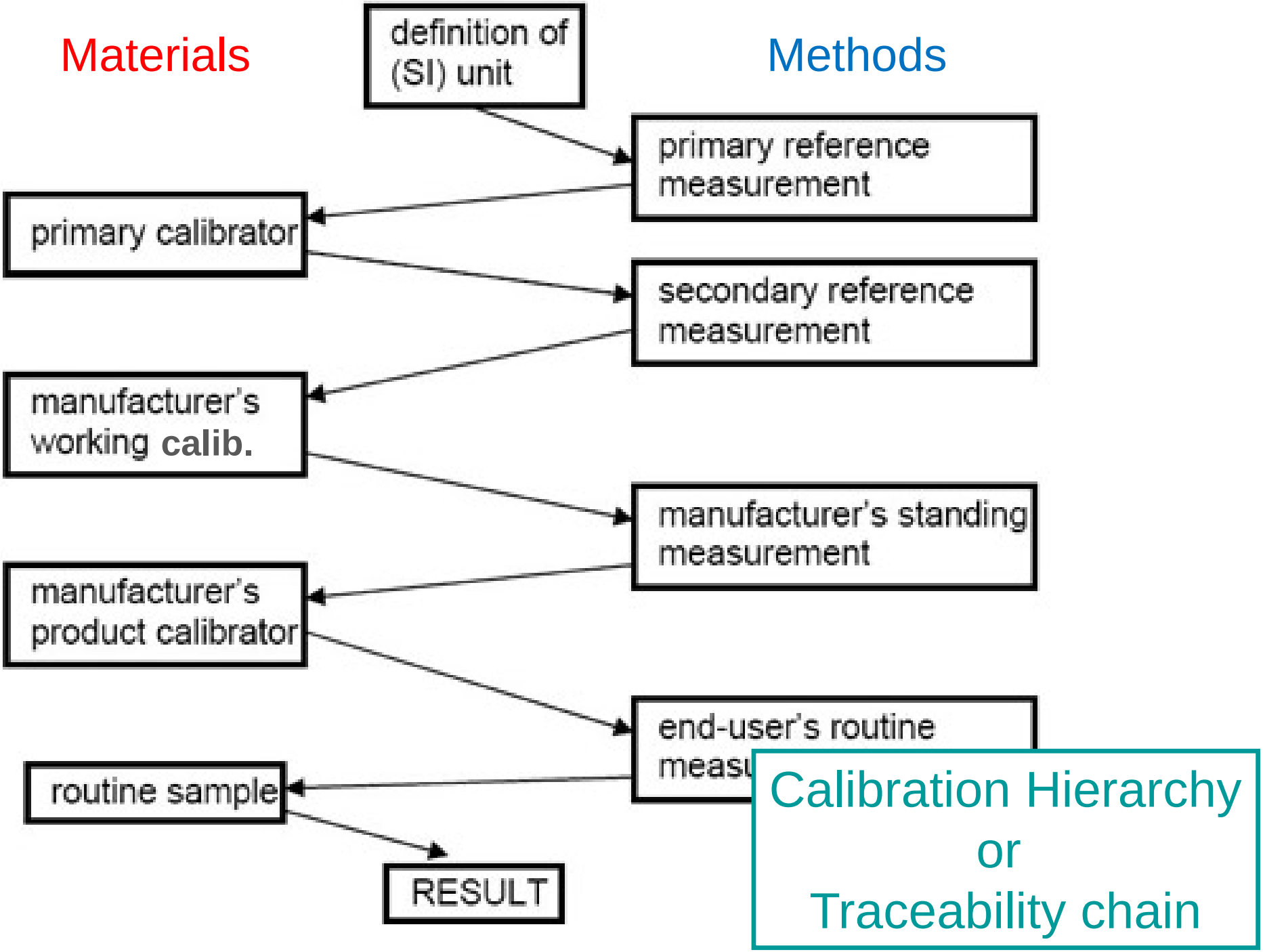
Laboratory Measurements

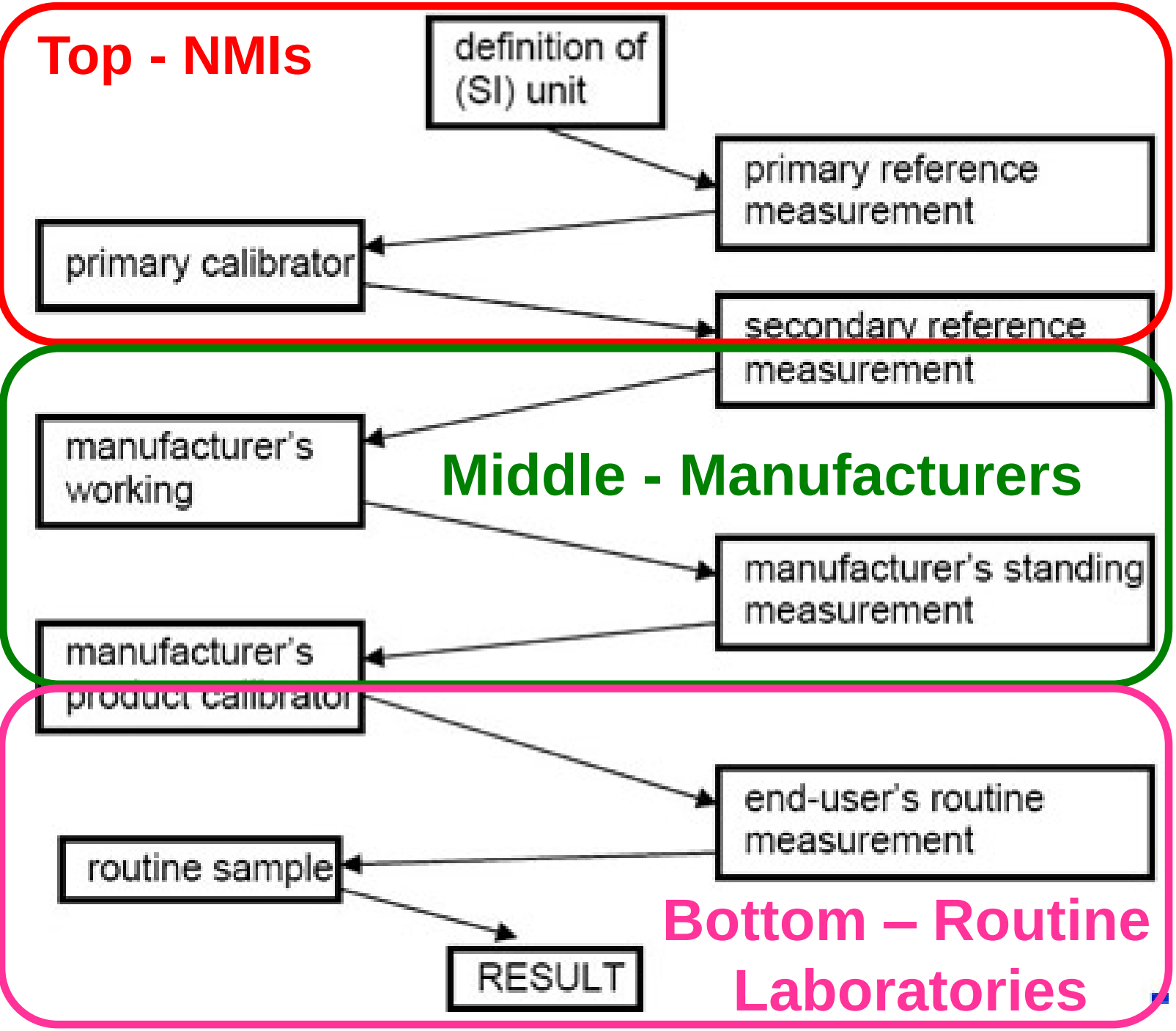
Laboratory Measurements

- All numerical **laboratory measurements** are made by **comparison**
- Analyte concentration in the **sample** is **compared** with concentration in the assay **calibrators**.
- **Calibrator values are assigned by traceability**



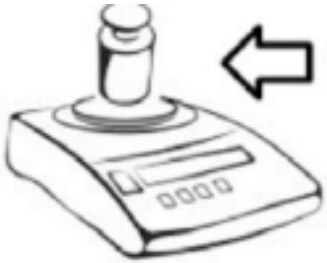


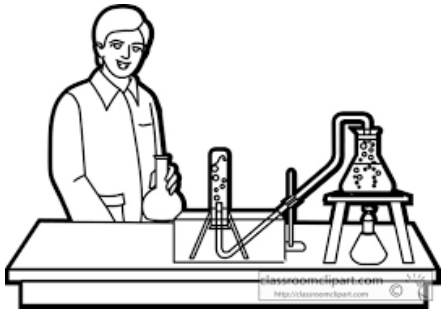

Materials
Methods
definition of (SI) unit
primary reference measurement
primary calibrator
secondary reference measurement
manufacturer's working calib.
manufacturer's standing measurement
manufacturer's product calibrator
end-user's routine
routine sample
RESULT
Calibration Hierarchy
or
Traceability chain


Top - NMIs
definition of (SI) unit
primary reference measurement
primary calibrator
secondary reference measurement
manufacturer's working
Middle - Manufacturers
manufacturer's standing measurement
manufacturer's product calibrator
end-user's routine measurement
routine sample
RESULT
Bottom – Routine Laboratories

The top of the traceability chain

- The top of the chain requires:
  - Material
  - Method
  - Laboratory





Joint Committee for Traceability in Laboratory Medicine (JCTLM)

- **JCTLM - Joining of:**
  - Metrology Community (BIPM)
  - Laboratory Medicine Community (IFCC)
  - Accreditation Community (ILAC)

- Aim to bring rigour and processes of metrology to laboratory medicine

Joint Committee for Traceability in Laboratory Medicine (JCTLM)

- **List of best:**
  - Reference Materials
  - Reference Methods
  - Reference laboratories
- **Promoting Traceability**
  - www.jctlm.org

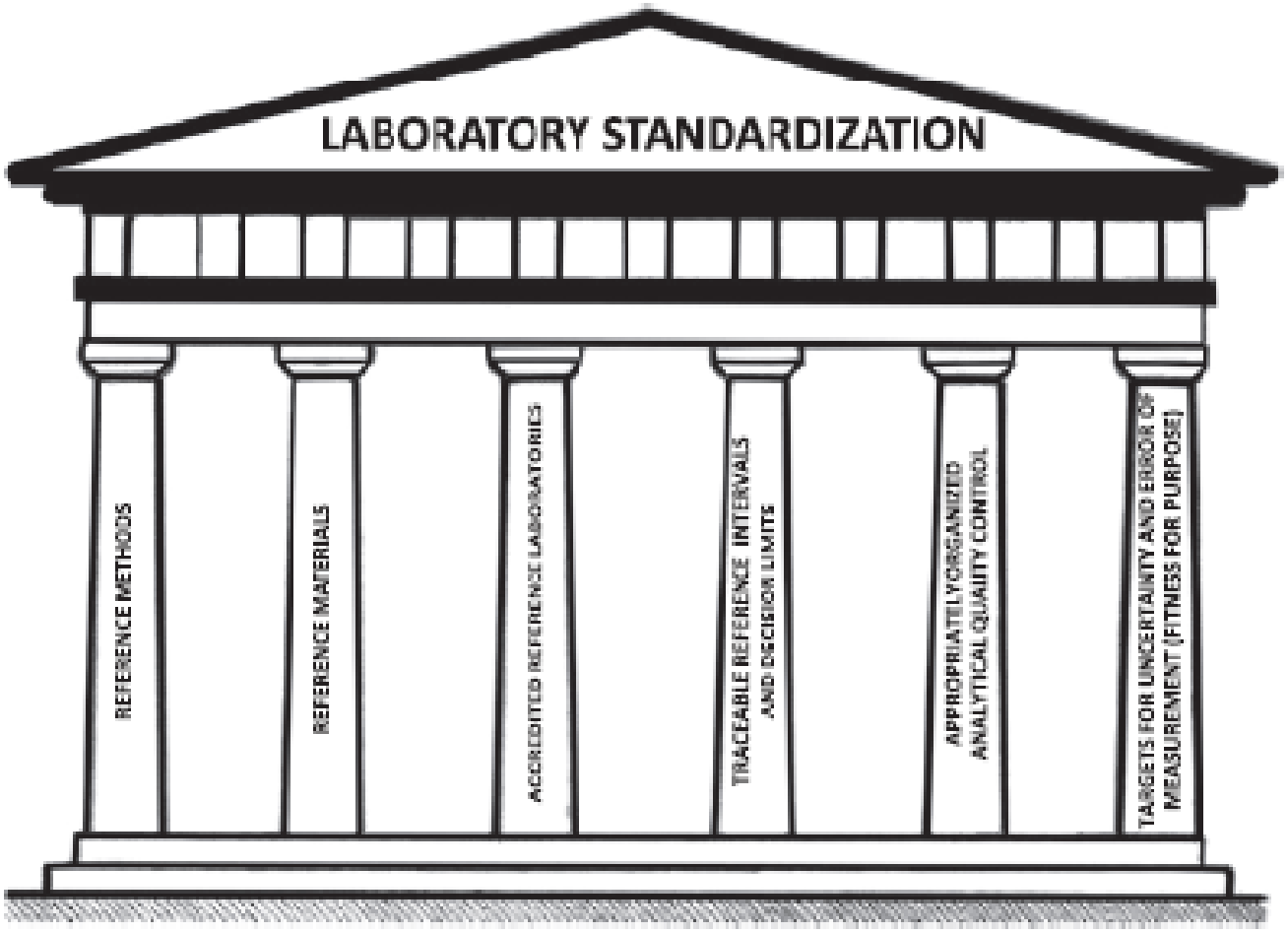
JCTLM
Accurate results for patient care

BIPM

ifcc
International Federation of Clinical Chemistry and Laboratory Medicine

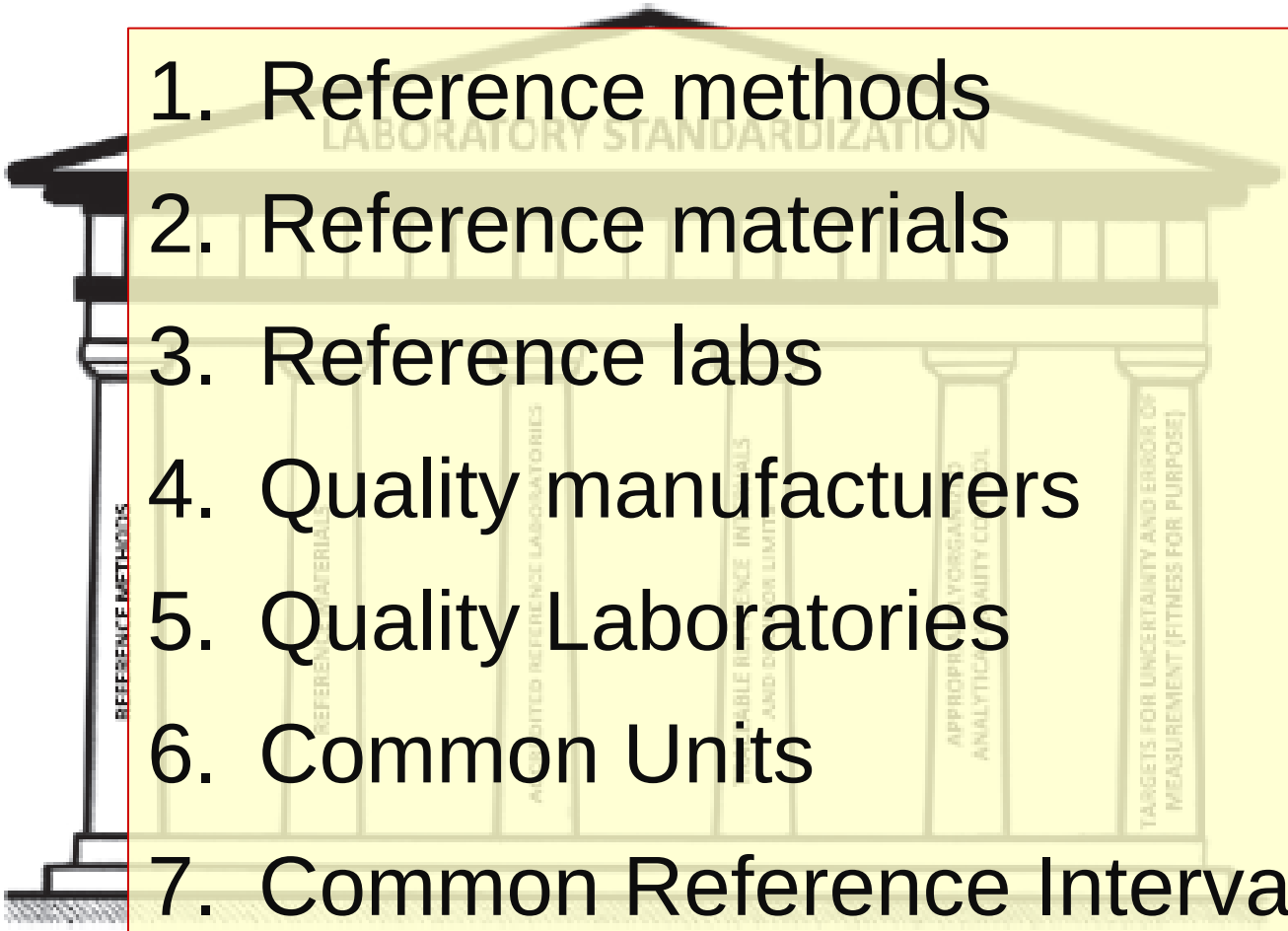
ilac

The temple of lab standardization – Pillars



Braga et al., CCA 2014

The temple of lab standardization – Pillars

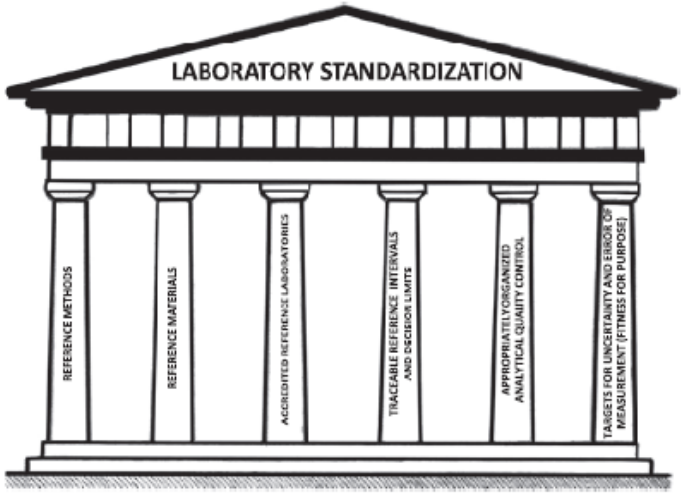


1. Reference methods
2. Reference materials
3. Reference labs
4. Quality manufacturers
5. Quality Laboratories
6. Common Units
7. Common Reference Intervals
8. External Quality Assurance

How are we going?

- Some tests fully traceable
- Some tests reasonable
- Some tests poor

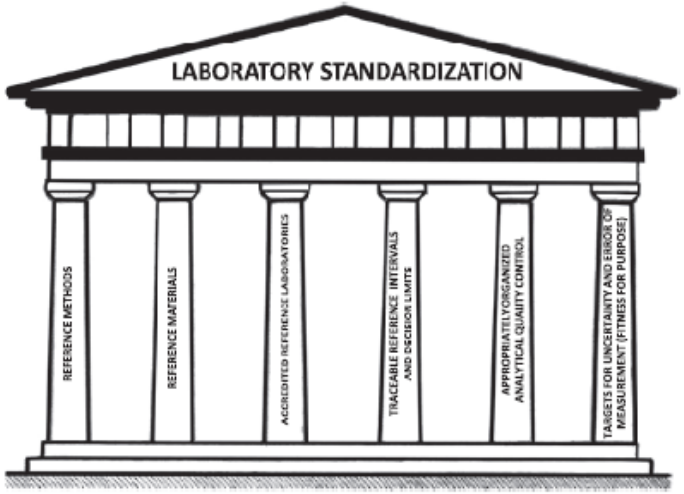
"I give us a B"



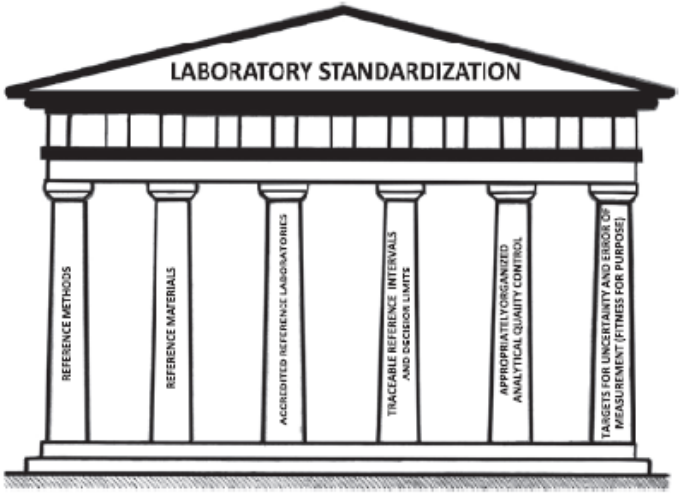
What is needed?

- More reference materials/methods
- Assay improvement by companies
- Laboratories selecting good assays
- Regulatory support
- Units, reference intervals, EQA etc

"lets get an A+"



- Thank you



(now back to the talk…)

What else is needed to benefit from traceable results?

- Terminology
- EQA
- Reference Intervals / Decision Points
- Identifying Traceable Results

Terminology

"***Traceability***" is a terrible term

- No one knows what it means
- It has other meanings
  (we mean metrological traceability)
- It is not descriptive of quality
  (all results are traceable)

JCTLM
Accurate results for patient care

JCTLM

JCTLM: Joint Committee for Trueness in Laboratory Medicine

JCCLM: Joint Committee for Comparability in Laboratory Medicine

JCELM: Joint Committee for Equivalence in Laboratory Medicine

JCALM: Joint Committee for Accuracy in Laboratory Medicine

JCULM: Joint Committee for Unbiased Results in Laboratory Medicine

Terminology

Describing a result as "***Traceable***" does not help

Suggest develop new term, eg:

"Verified Traceable" result

- Claimed traceability to appropriate higher order references
- Uncertainty with specified limits
- Verified with EQA

The Role of External Quality Assurance

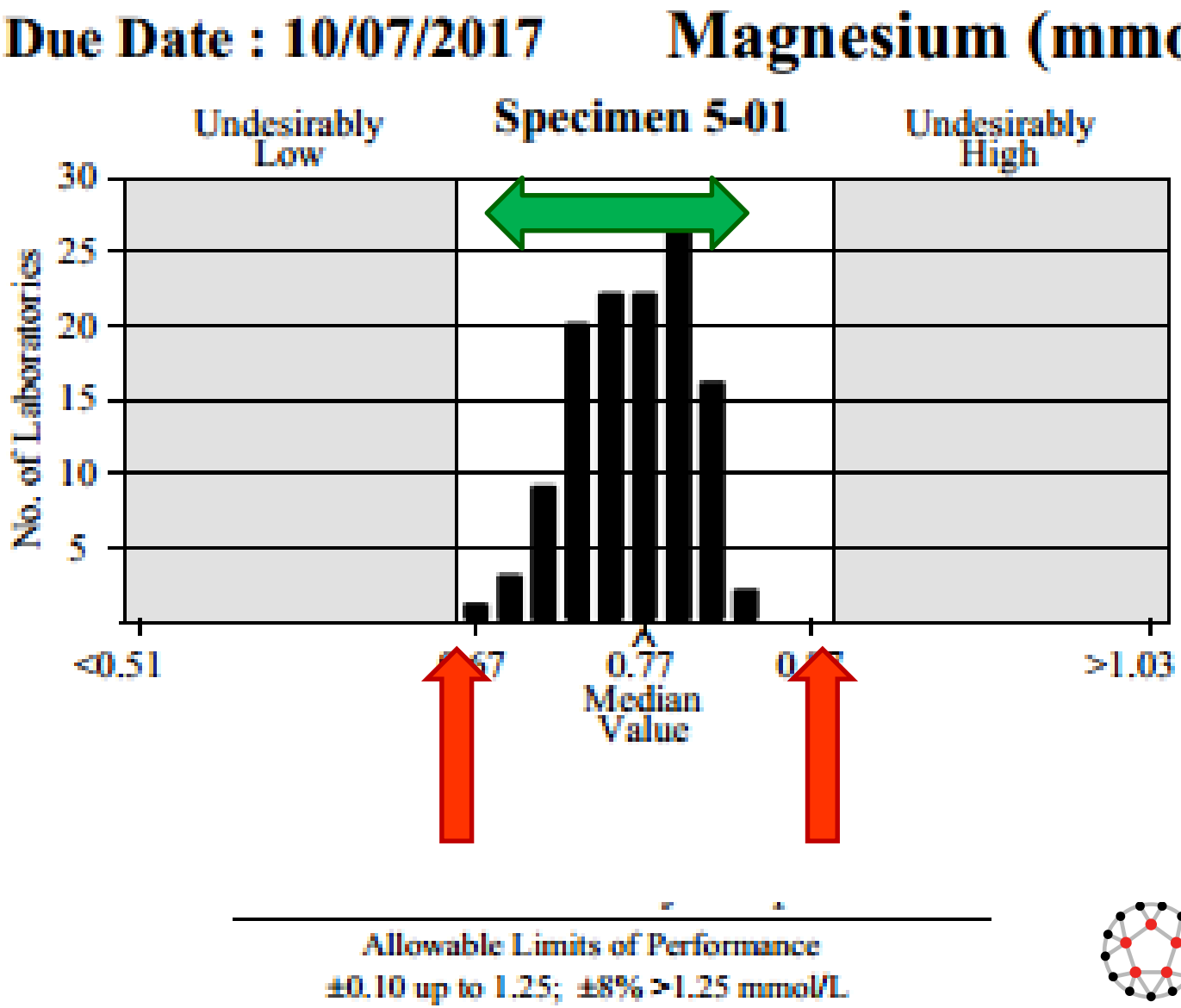
- Inherent in *traceability* is *uncertainty*
  Inherent in *measurement traceability* is *measurement uncertainty*
- Traceable results from different labs ***will*** vary:
- Differences due to:
  - Different reference materials/ methods
  - Expected uncertainty in traceability chains
  - Unexpected uncertainty (e.g. non-commutability)
- Key questions:
  - Different by how much?
  - Is this difference important?

The Role of External Quality Assurance

- ***Results*** of EQA say how different

- EQA ***Performance Specifications*** say whether difference is important

RCPAQAP – Commutable serum

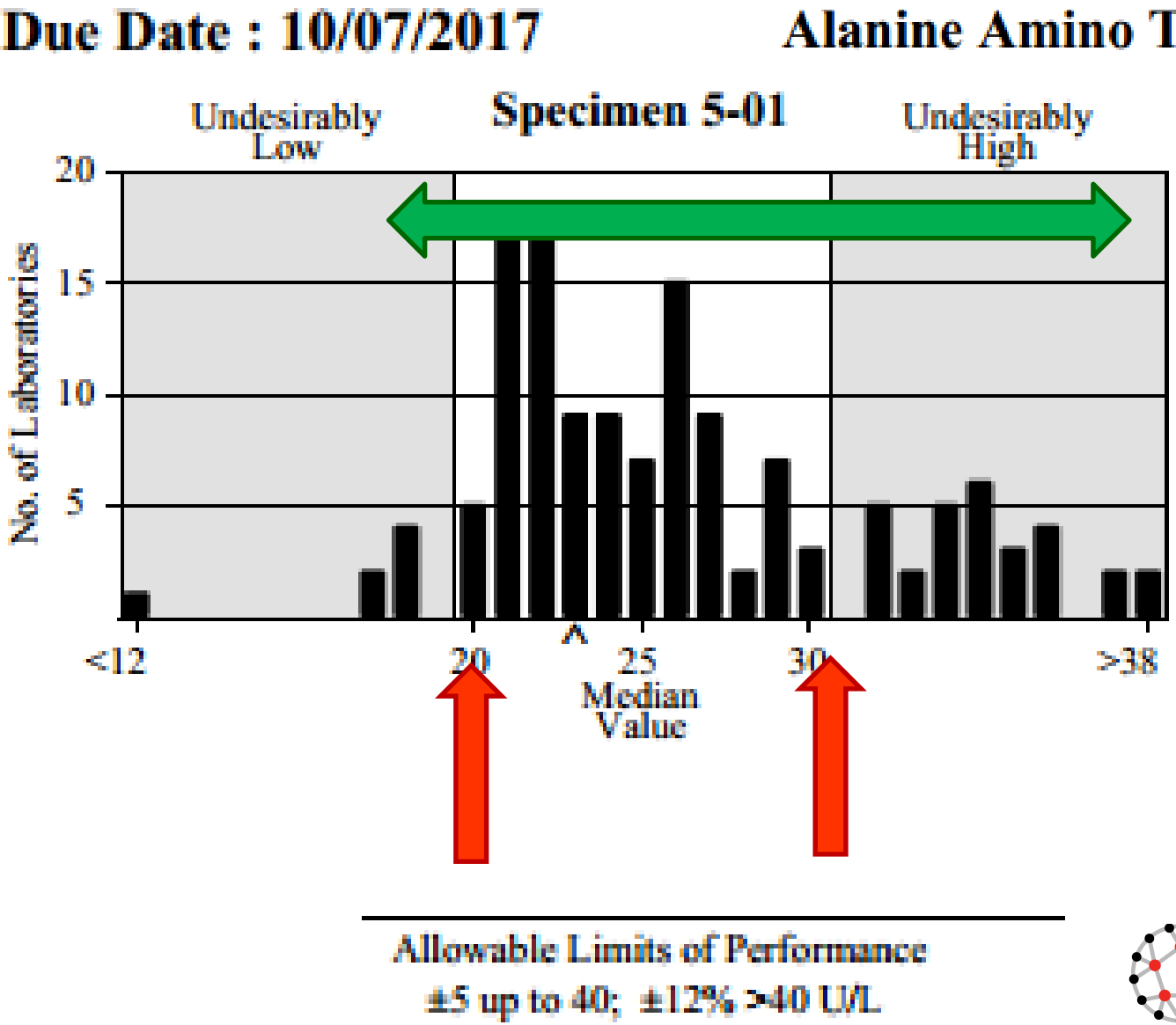


How Different

How Good

RCPAQAP
RCPA Quality Assurance Programs

RCPAQAP – Commutable serum



How Different

How Good

RCPAQAP
RCPA Quality Assurance Programs

Milan 2014

DE GRUYTER

Clin Chem Lab Med 2015; 53(6): 833–835

Consensus Statement

Sverre Sandberg*, Callum G. Fraser, Andrea Rita Horvath, Rob Jansen, Graham Jones, Wytze Oosterhuis, Per Hyltoft Petersen, Heinz Schimmel, Ken Sikaris and Mauro Panteghini

Defining analytical performance specifications: Consensus Statement from the 1st Strategic Conference of the European Federation of Clinical Chemistry and Laboratory Medicine

Milan 2014

- *Model 1 - Based on the effect of analytical performance on clinical outcomes*
- *Model 2 - Based on components of biological variation of the measurand*
- *Model 3 - Based on state of the art*

DE GRUYTER Clin Chem Lab Med 2015; 53(6): 919–924

Opinion Paper

Graham Ross Dallas Jones*

Analytical performance specifications for EQA schemes – need for harmonisation

Clin Chem Lab Med 2015; 53(6): 919–924

EQA Performance Specifications - 2017

DE GRUYTER

Clin Chem Lab Med 2017; aop

Opinion Paper

Graham R.D. Jones*, Stephanie Albarede, Dagmar Kesseler, Finlay MacKenzie, Joy Mammen, Morten Pedersen, Anne Stavelin, Marc Thelen, Annette Thomas, Patrick J. Twomey, Emma Ventura and Mauro Panteghini, for the EFLM Task Finish Group – Analytical Performance Specifications for EQAS (TFG-APSEQA)

Analytical performance specifications for external quality assessment – definitions and descriptions

Clin Chem Lab Med 2017; 55(7): 949–955

EFLM
EUROPEAN FEDERATION OF CLINICAL CHEMISTRY AND LABORATORY MEDICINE

Elements of APS Terminology

To interpret EQA Analytical Performance Specifications, we need to describe:

1) EQA material and commutability;
2) Method used to assign the target value;
3) Data set to which APS are applied;
4) Analytical property being assessed (i.e. total error, bias, imprecision);
5) Rationale for the selection of the APS;
6) Milan model(s) used to set APS.

Jones et al, Clin Chem Lab Med 2017; 55(7): 949–955

Reference Intervals

- The ***comparator*** is as important as the ***result***

- **For results we:**
  - Validate methods
  - Control daily (or more) with QC
  - Check monthly (or more) with EQA
  - Troubleshoot problems in real time

- How good are our **comparators?**

Commentary

RCPAQAP First Combined Measurement and Reference Interval Survey

Graham RD Jones[1,2], Sabrina DA Koetsier[2]

[1]SydPath, St Vincent's Hospital, Sydney and [2]RCPAQAP Chemical Pathology, Adelaide, Australia

*For correspondence: Dr Graham Jones, Graham.Jones@svha.org.au

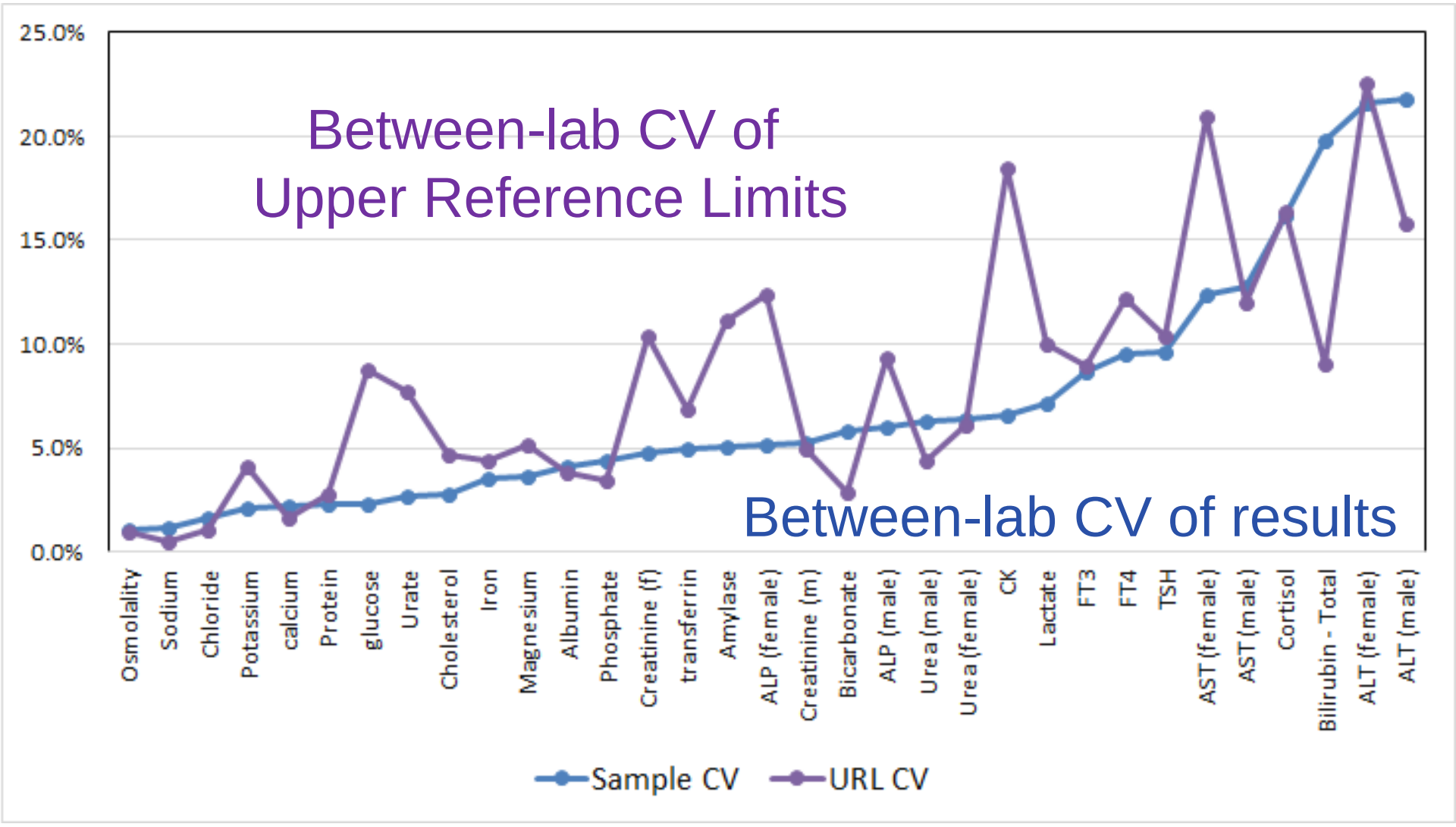
Clin Biochem Rev 35 (4) 2014 243

RCPAQAP
RCPA Quality Assurance Programs

Reference Interval Survey

- Variation in Reference Intervals
  - **MORE than analytical differences**
- Were Differences in Reference Intervals due to assay bias
  - **No**
- Did differences in Intervals increase or decrease diagnostic accuracy
  - **Decrease**

RCPAQAP
RCPA Quality Assurance Programs


Between-lab CV of
Upper Reference Limits
Between-lab CV of results
25.0%
20.0%
15.0%
10.0%
5.0%
0.0%
Osmolality
Sodium
Chloride
Potassium
calcium
Protein
glucose
Urate
Cholesterol
Iron
Magnesium
Albumin
Phosphate
Creatinine (f)
transferrin
Amylase
ALP (female)
Creatinine (m)
Bicarbonate
ALP (male)
Urea (male)
Urea (female)
CK
Lactate
FT3
FT4
TSH
AST (female)
AST (male)
Cortisol
Bilirubin - Total
ALT (female)
ALT (male)
Sample CV
URL CV

Canadian Reference Intervals Survey

National Survey of Adult and Pediatric Reference Intervals in Clinical Laboratories across Canada: A Report of the CSCC Working Group on Reference Interval Harmonization

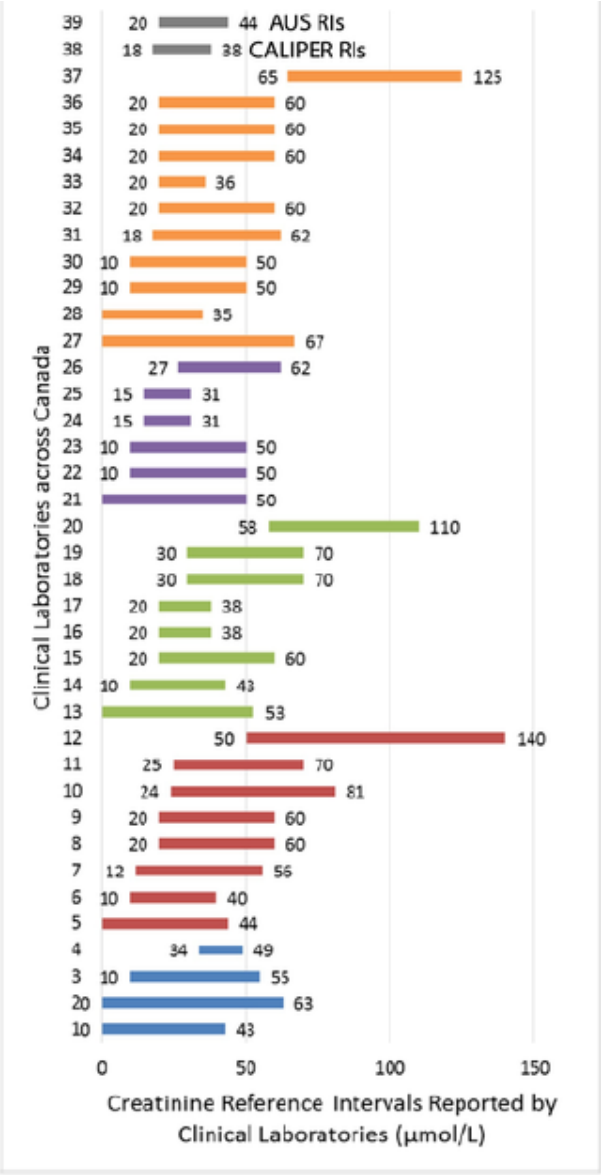
Khosrow Adeli[a,*], Victoria Higgins[a], David Seccombe[b], Christine P. Collier[c], Cynthia Balion[d], George Cembrowski[e], Allison A. Venner[f], Julie Shaw[g]on behalf of the CSCC Reference Interval Harmonization (hRI) Working Group

Clinical Biochemistry

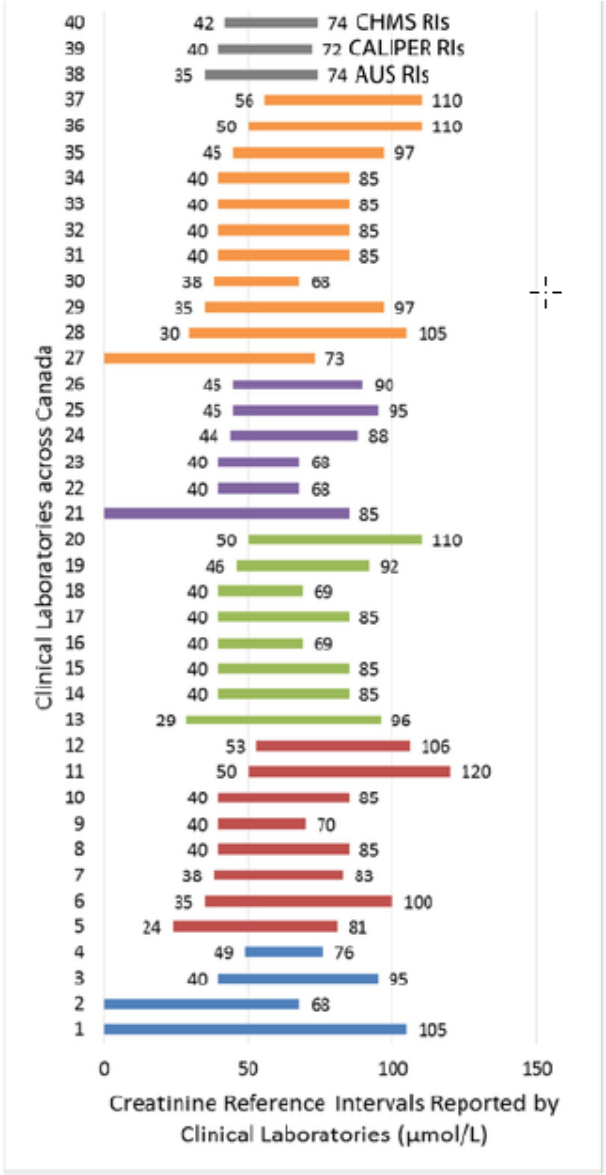
Volume 50, Issues 16–17, November 2017, Pages 925-935

Serum Creatinine Reference Intervals

2 year old male



14 year old female



50 year old male

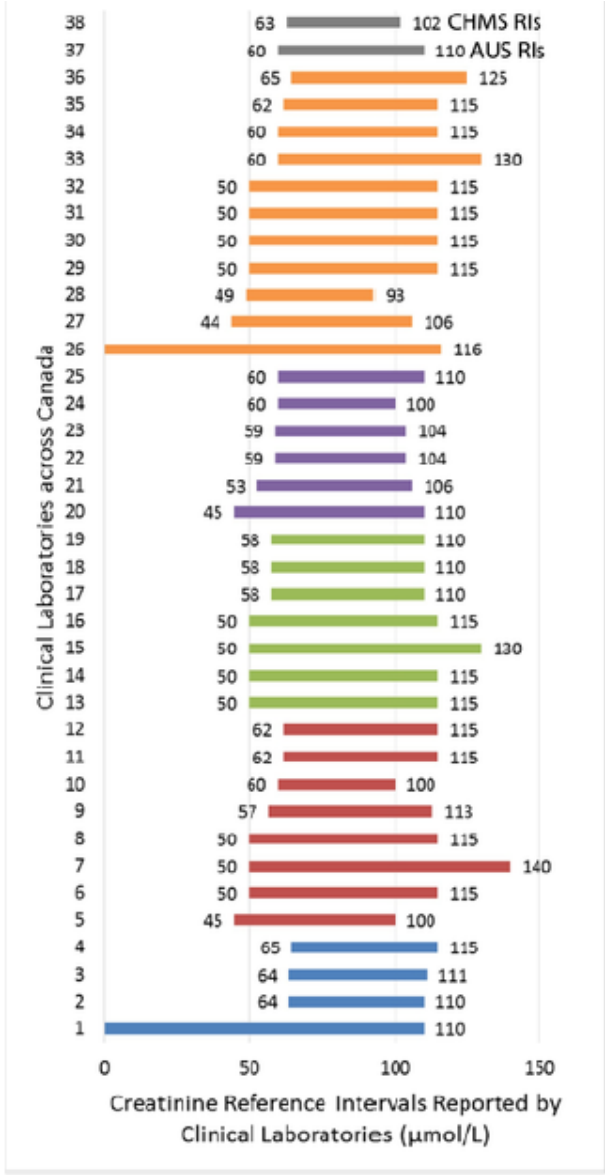


Table 2
Comparing variation and bias between reference sample results and reference intervals.

Analyte	Instrument	CV_{BL}	%V (LRL)	%V (URL)
ALT, U/L	All	24.6%		**30.2%**
	Abbott	7.5%		**21.9%**
	Beckman	15.0%		**20.4%**
	Ortho	5.3%		**22.6%**
	Roche	9.7%		6.4%
	Siemens	19.7%		**36.8%**
ALP, U/L	All	6.6%		**41.9%**
	Abbott	3.8%	**18.2%**	**52.3%**
	Beckman	5.2%	**46.5%**	**35.7%**
	Ortho	2.1%	**41.7%**	**43.2%**
	Roche	2.8%		**23.1%**
	Siemens	3.1%		**41.1%**

Adeli K et al. Clin Biochem 2017

Common Reference Intervals

- Australian Project
- 2013 – 2015 (ongoing)
  - 12 Common tests
  - Sodium, Potassium, Calcium …

aacb
testing for health

RCPA
The Royal College of Pathologists of Australasia

RCPAQAP
RCPA Quality Assurance Programs

1st Common Reference Intervals

Clinical Biochemist Reviews – 2014;35:213-235

Special Report

Harmonising Adult and Paediatric Reference Intervals in Australia and New Zealand: An Evidence-Based Approach for Establishing a First Panel of Chemistry Analytes

***Jillian R Tate,[1] Ken A Sikaris,[2] Graham RD Jones,[3] Tina Yen,[4] Gus Koerbin,[5] Julie Ryan,[6] Maxine Reed,[7] Janice Gill,[8] George Koumantakis,[9] Peter Hickman,[10] Peter Graham,[11] on behalf of the AACB Committee for Common Reference Intervals**

Analyte	Male	Female
Calcium	2.15 – 2.55 mmol/L	
Phosphate	0.75 – 1.50 mmol/L	
Magnesium	0.7 – 1.1 mmol/L	
LDH [L to P]IFCC	120 – 250 U/L	
Sodium	135 – 145 mmol/L	
Potassium	3.5 – 5.2 mmol/L	
Chloride	95 – 110 mmol/L	
Bicarbonate	22 – 32 mmol/L	
Creatinine	60 – 110 umol/L	45 – 90 umol/L
ALP	30 – 110 U/L	
AST	<40	<35
ALT	<40	<30
Total Protein	60 – 80 g/L	

towards global harmonisation

Short Report

The Association for Clinical Biochemistry & Laboratory Medicine
Better Science, Better Testing, Better Care

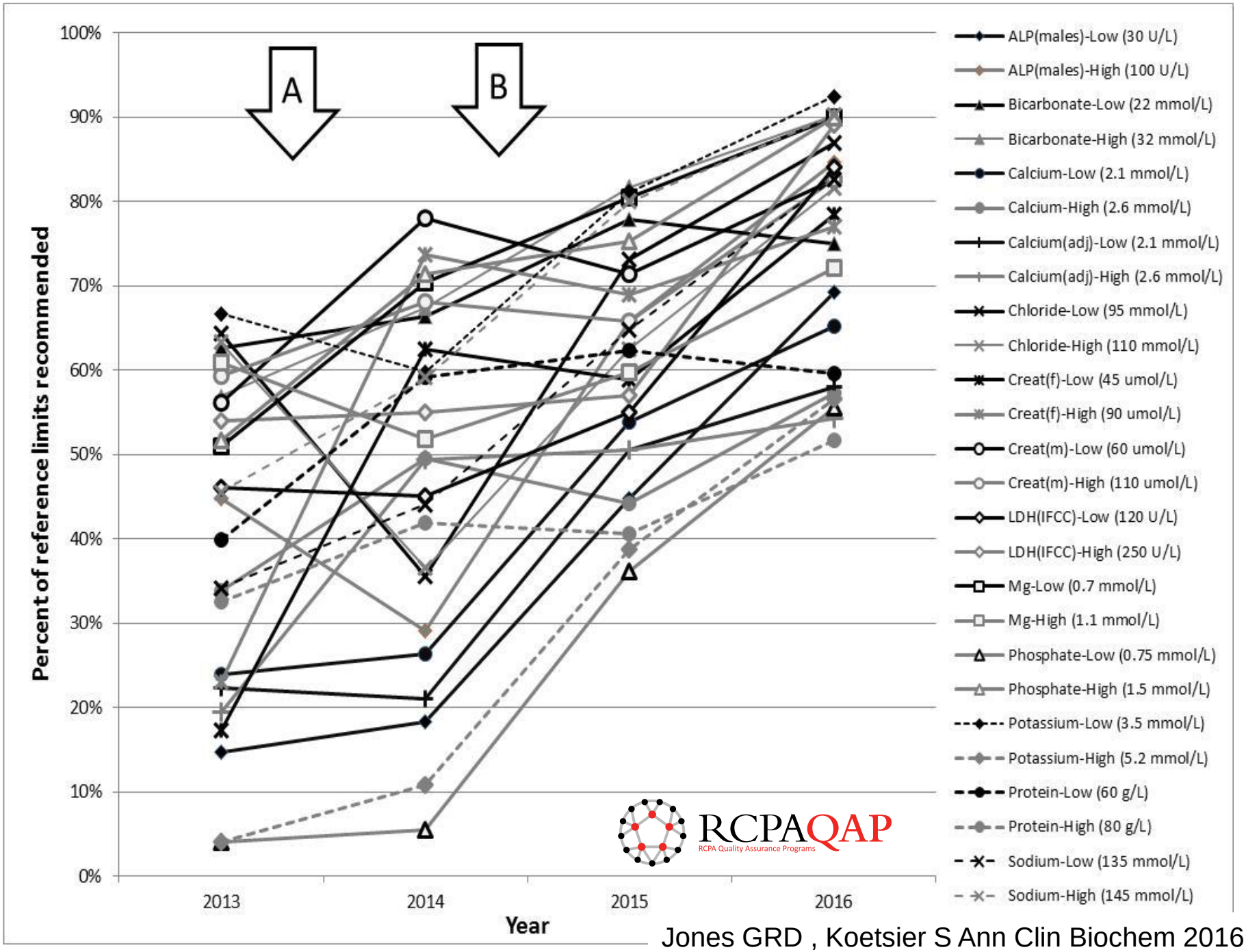
Annals of Clinical Biochemistry
2017, Vol. 54(3) 395–397

DOI: 10.1177/0004563216679853
journals.sagepub.com/home/acb
SAGE

Uptake of recommended common reference intervals for chemical pathology in Australia

Graham RD Jones[1,2] and Sabrina Koetsier[3]

RCPAQAP
RCPA Quality Assurance Programs



Jones GRD , Koetsier S Ann Clin Biochem 2016

Comparators:

- Benefits of traceability only delivered where comparators are also traceable
  - Reference intervals
  - Clinical decision points (guidelines)
  - Results from Other laboratories

- Improvements required
  - Using traceable methods for studies
  - Awareness of differences
  - Specialist involvement with guidelines

Using Traceable Results

- When interpreting (comparing) results – the user needs to know whether the patient results are comparable to the reference results
- This needs either:
  - All results (for a measurand) to be traceable
    - The ideal
    - Possible: Glucose, cholesterol HbA1c
  - Nomenclature / tools for identifying traceability
    - Test names eg AST (IFCC)
    - Coding (eg LOINC) for combining in displays (LOINC codes for traceable methods?)

Are My Results Traceable?

- **Manufacturers**
  - Better descriptions in IFU
  - Reference JCTLM where relevant (a *"trusted brand"*)
- **Test Names for "Verified Traceable" results**, eg:
  - AST (IFCC)
  - AST (JCTLM)
  - AST (non-traceable) (name by exclusion)
- **Coding for IT Systems**
  - eg LOINC code for "verified traceable" results
  - Only combine traceable results in databases

Traceability for the public

- Every civilisation and every craft has its tools for spreading measurement standards
- Traceability is the modern version
- It is vital we apply this to Laboratory Medicine
- There are many steps still to take …