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UNIVERSITÀ DEGLI STUDI DI MILANO

Redesigning Internal Quality Control to obtain information about metrological traceability of IVD-MDs and associated measurement uncertainty

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Clinical Pathology Unit
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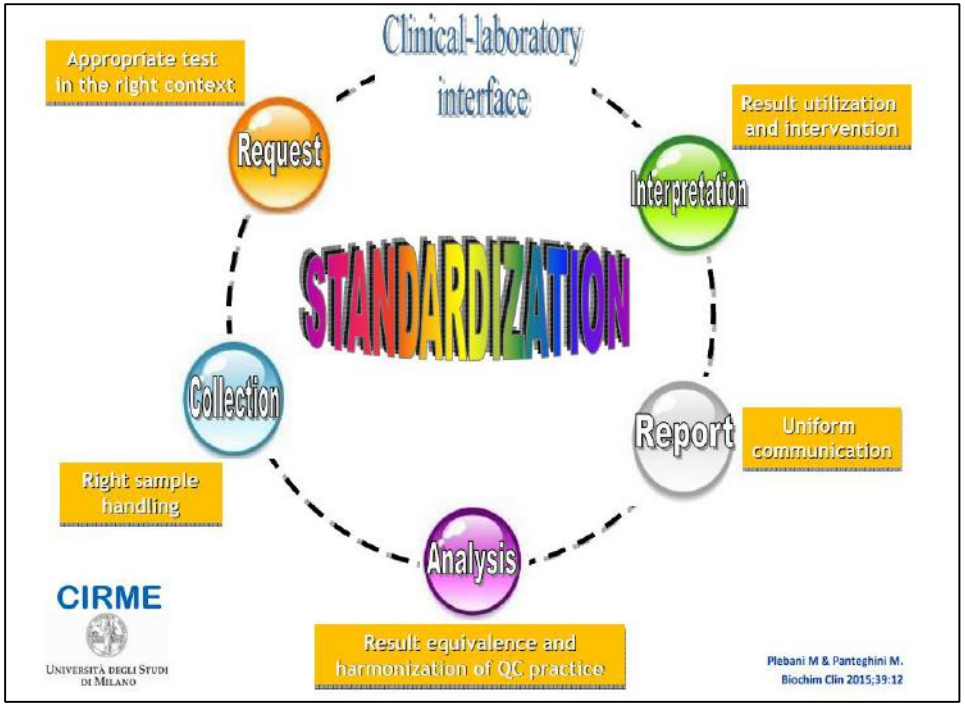
International Scientific Meeting
Evaluating and monitoring analytical quality in the traceability era
Bydgoszcz, November 29th 2024

STANDARDIZATION



"Standardization of laboratory tests has an ethical dimension as it aims to affect the way diagnostic tests are used in order to guarantee optimal care for patients in a global world."

Bossuyt X et al., Ann Rheum Dis 2008;67:1061

A MATTER OF PATIENT SAFETY!!

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STANDARDIZATION

Laboratory Medicine is clinically effective when the provided information can be interpreted in a reliable and consistent manner

LABORATORY RESULTS

ACCURATE

Tolerable measurement error without jeopardizing patient safety

EQUIVALENT

[For long term] No matter where they are performed

TRACEABILITY IMPLEMENTATION

Results obtained by the calibrated commercial procedure expressed in terms of the values obtained at the highest available level of the calibration hierarchy

TRACEABILITY IMPLEMENTATION

PROFESSION
(e.g., IFCC, JCTLM)

DIAGNOSTIC MANUFACTURERS

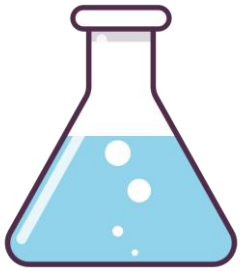
Implement suitable measuring systems (platform, reagents, calibrators, controls)

Define analytical objectives: reference measurement systems (traceability chain) and associated clinically acceptable uncertainty (fit for purpose)

END USERS
(clinical laboratories)

Survey assay and laboratory performance through IQC and EQA redesigned to meet metrological criteria

Responsibilities of clinical labs

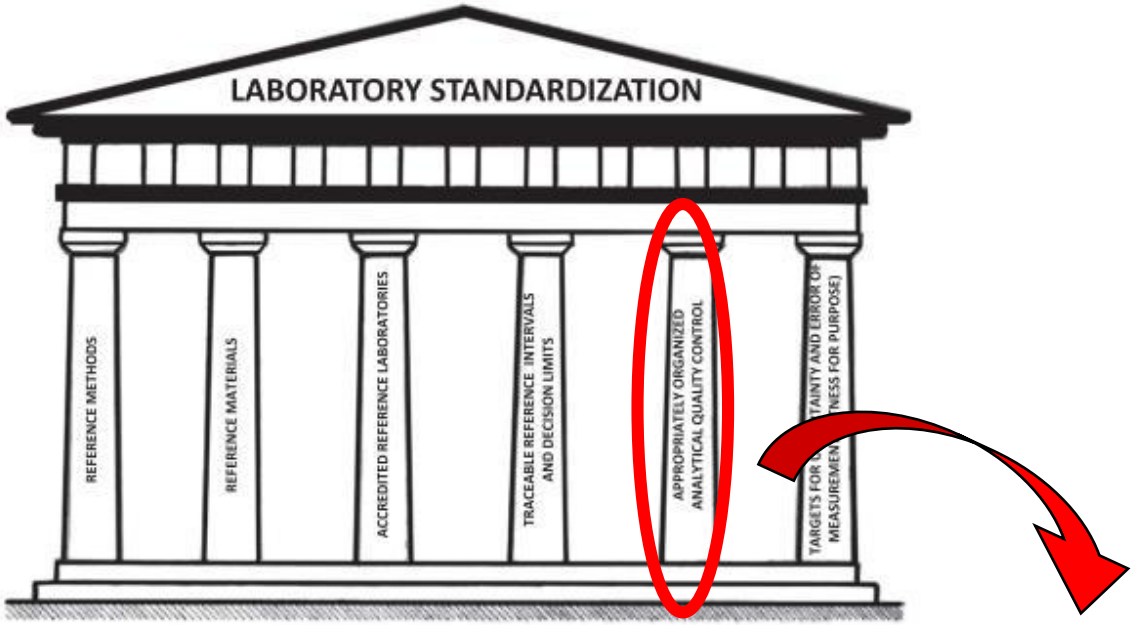


1. Verify the availability and the quality of available **INFORMATION** about the metrological traceability and uncertainty of employed IVD system

2. Perform **SURVEILLANCE** of the employed IVD system traceability

3. Estimate **MEASUREMENT UNCERTAINTY** due to random error (IQC component II) and calculate total MU of patient results

REDESIGNING IQC



Braga F & Panteghini M, Clin Chim Acta 2014;432:55

An *<u>appropriately organized</u>* analytical (internal and external) quality control program, redesigned to meet metrological concepts, has been recognized as *<u>one of the key elements of laboratory standardization</u>*

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Clin Chem Lab Med 2021; 59(2): 291–300

REDESIGNING IQC

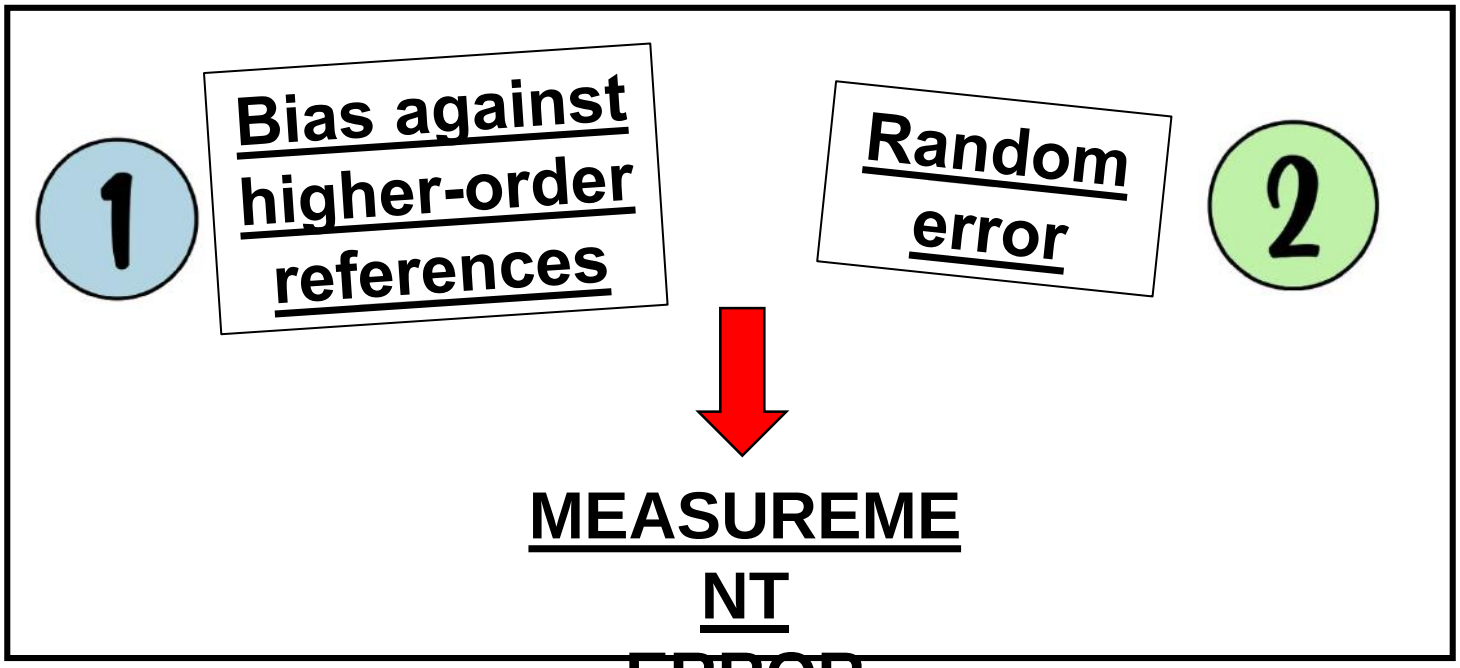
Clin Chem Lab Med 2010;48(1):7–10 © 2010 by Walter de Gruyter • Berlin • New York. DOI 10.1515/CCLM.2010.020

Editorial

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

The need to apply metrological traceability concepts to the analytical QC for surveying assay standardization was pointed out 14 years ago

SOURCES OF ERROR

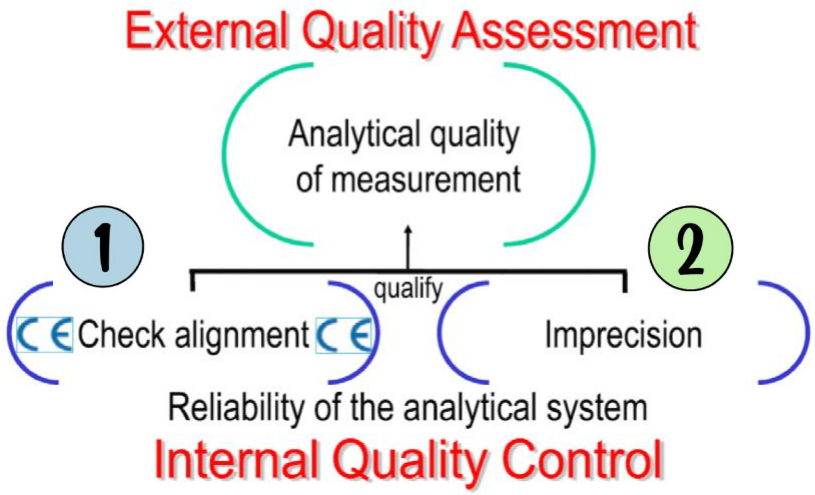


"medical laboratories should (…) establish and maintain routines for estimating and minimizing them separately"

Oosterhuis WP et al. Clin Chem Lab Med 2018;56:209–19

REDESIGNING IQC

Analytical Quality Control in the Traceability Era



Components I & II are independent

1 IQC Component I

- Check alignment of the measuring system
- Verify consistency of declared traceability during routine operations performed in accordance with the manufacturer's instructions

2 IQC Component II

- Estimate the measurement uncertainty due to random effects

IQC COMPONENT I

Key responsibilities of IVD manufacturers in order to fulfill the EU IVD Directive and REGULATION (EU) 2017/746 Requirements about traceability to higher-order references.

- Identification of appropriate higher-order metrological references
- Definition of a calibration hierarchy to assign traceable values to measuring system calibrators and bias correction during the trueness transfer process
- Estimation of combined measurement uncertainty of calibrators
- Fulfillment of measurement uncertainty specifications for calibrators, which represent a proportion of the uncertainty budget allowed for medical laboratory results

[Braga F & Panteghini M, Clin Chim Acta 2014;432:55]

STUFF HAPPENS!!

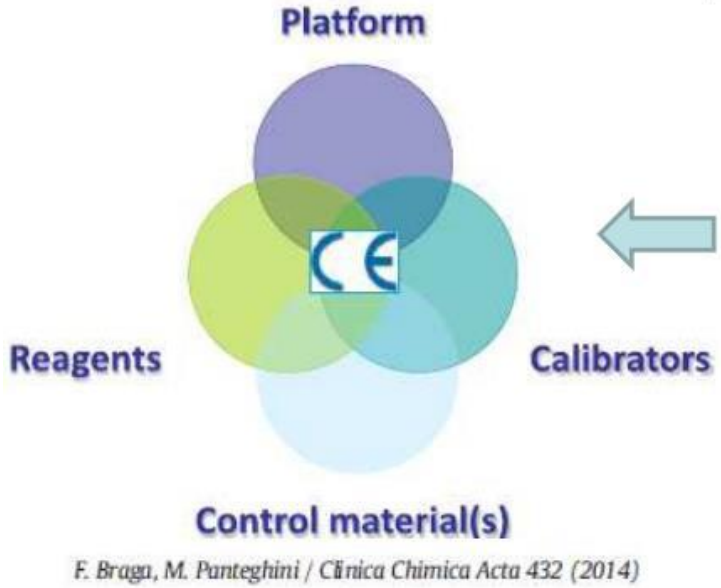
GOAL of IQC component I:

To monitor acceptability of changes in system alignment which might intervene during daily activity

IQC COMPONENT I

Measuring System Components in the Traceability Era

The Paradigm Shift

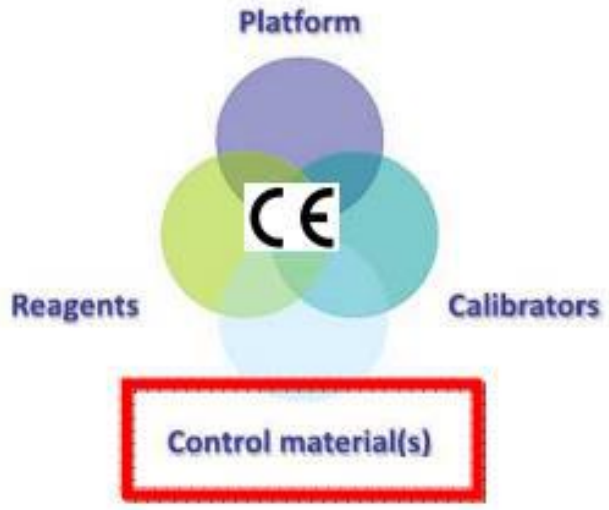


F. Braga, M. Panteghini / Clinica Chimica Acta 432 (2014)

If the manufacturer should assume total responsibility for supplying products of acceptable quality in terms of traceability and uncertainty of the system ("CE marked"), it is no longer possible to consider separately the components of each analytical system (i.e., platform, reagents, calibrators and control materials), which in terms of performance can only be guaranteed and certified by the manufacturer as a whole.

Changes introduced by users or third parties (e.g., the use of reagents, calibrators or control materials from other suppliers) may significantly alter the quality of the analytical system performance, removing any responsibility from the manufacturer and depriving the system (and, consequently, the produced results) of the certification originally provided through CE marking.

IQC COMPONENT I



- The IQC-I material **must be provided by the IVD** manufacturer as an integral part of the CE marked analytical system and must be used by the laboratory **in accordance with manufacturer's indications**.
- *If the traceability of the measuring system to higher-order references is granted*, control materials from the IVD manufacturers **have to be a good surrogate of the employed (and declared) reference** to permit checking the correct system alignment to this reference

IVD manufacturers should therefore provide end-users with materials with appropriate target values and acceptability ranges, designed for daily surveillance of the system alignment, when working according to the manufacturer's indications

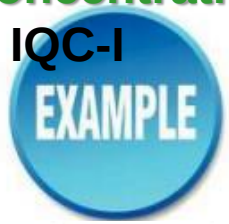
IQC COMPONENT I

MAIN CHARACTERISTICS OF QUALITY CONTROL MATERIAL FOR SYSTEM ALIGNMENT VERIFICATION

- **Concentration levels** in line with clinically relevant thresholds
- **Unbiased** target value
  (note that commutable materials are not required because materials are produced to be used on a specific measuring system, with the possibility of matrix-related bias)
- **Acceptability range** according to the suitable application of test results in clinical setting
- Enough stability to monitor the performance of the measuring system under the influence of components potentially deteriorating it

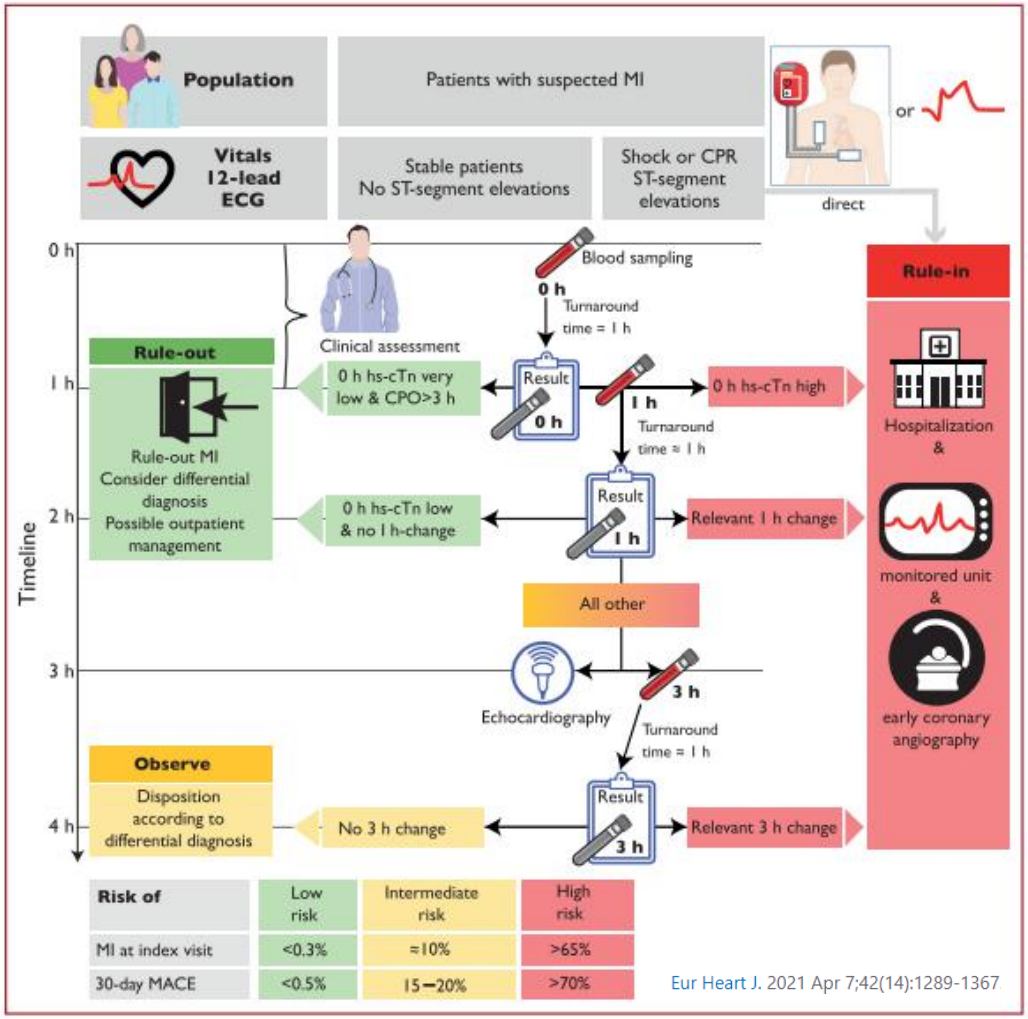
IQC COMPONENT I

Why are clinically relevant measurand concentrations important for IQC-I materials?



0 h/1 h algorithm	Very low
hs-cTn T (Elecsys; Roche)	<5
hs-cTn I (Architect; Abbott)	<4
hs-cTn I (Centaur; Siemens)	<3
hs-cTn I (Access; Beckman Coulter)	<4
hs-cTn I (Clarity; Singulex)	<1
hs-cTn I (Vitros; Clinical Diagnostics)	<1
hs-cTn I (Pathfast; LSI Medience)	<3
hs-cTn I (TriageTrue; Quidel)	<4
0 h/2 h algorithm	**Very low**
hs-cTn T (Elecsys; Roche)	<5
hs-cTn I (Architect; Abbott)	<4
hs-cTn I (Centaur; Siemens)	<3
hs-cTn I (Access; Beckman Coulter)	<4
hs-cTn I (Clarity; Singulex)	<1
hs-cTn I (Vitros; Clinical Diagnostics)	<1
hs-cTn I (Pathfast; LSI Medience)	<3
hs-cTn I (TriageTrue; Quidel)	<4

ESC 0h/1h algorithm for rule-in/rule-out of AMI



Eur Heart J. 2021 Apr 7;42(14):1289-1367

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IQC COMPONENT I

Why are clinically relevant measurand concentrations important for IQC-I materials?

"In the clinical scenario described in ESC recommendations for early NSTEMI ruling out at patient admission, accurate calibration of hs-cTn assays in the very low range of concentrations is of the upmost importance as even relatively small analytical misalignments in practice may influence the proportion of patients identified as suitable for discharge (…)

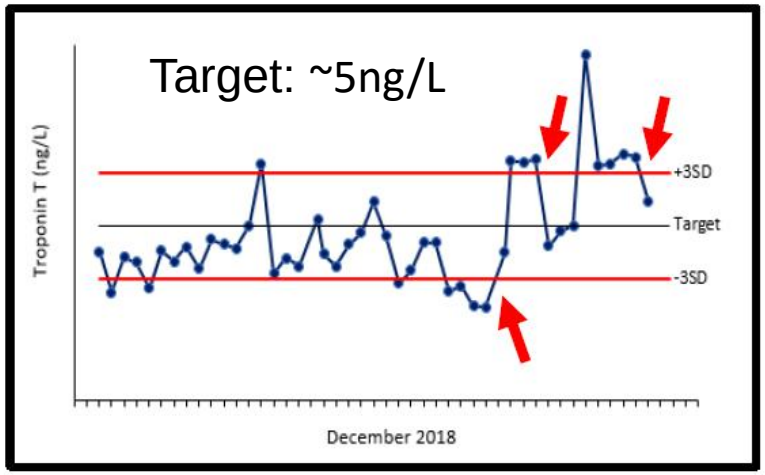
However, commercial control materials supplied by manufacturers do not cover such very low cTn concentrations, making the assay susceptible to undetected drifts. "

IQC COMPONENT I

Why are clinically relevant measurand concentrations important for IQC-I materials?

Daily monitoring of a control material with a concentration near the limit of detection improves the measurement accuracy of highly sensitive troponin assays

Clin Chem Lab Med 2020; 58(2): e29–e31



EQAS program for low-concentration cTn:
results **PRE**-«very low IQC»: 40,0% failure rate
results **POST**-«very low IQC»: 3,8% failure rate

If results are "**out of control**", immediate **corrective actions** are implemented **before reports** related to the samples analysed in the affected run **are issued**.

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IQC COMPONENT I

Why is an unbiased target value for IQC-I materials important?

For effective surveillance of traceability, IQC-I target values must be assigned by the manufacturer by performing replicate measurements on the same measuring system, optimally calibrated to the declared reference, in order to confirm that the measuring system performance is properly unbiased.

ASSIGNMENT OF VALUES

The values provided in the data sheet were derived from replicate analyses and are specific for a particular lot of product. These values have been generated using third party manufacturers' instrument systems and are specific to one measurement procedure. [redacted] make no accuracy claims regarding these values. Tests were performed by the control manufacturer and/or by independent laboratories, for various methods and instrument systems. As a tool to assist in establishing their own mean, laboratories can import the values into their [redacted] system. For more details and to register for access to this file please visit www.[redacted].com.

Values are provided only as guidelines, each laboratory should establish its own statistical limits. Laboratory means may vary from the values listed during the shelf life of the control. [redacted] monitors the values over the shelf life of the control and provides update(s) at www.[redacted].com or contact your local [redacted] customer service representative.

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IQC COMPONENT I

Why is an unbiased target value for IQC-I materials important?

... Mean value derived from replicate performed by independent laboratory

... Data from interlaboratory program are included in the determination of some ranges

... Values/Range provided only as guides

... Values listed are approximate targets and are provided only for convenience

... No accuracy claims regarding mean value

... Values update during the shelf life of the material available @website

... Each laboratory should establish its own statistical limits

IQC COMPONENT I

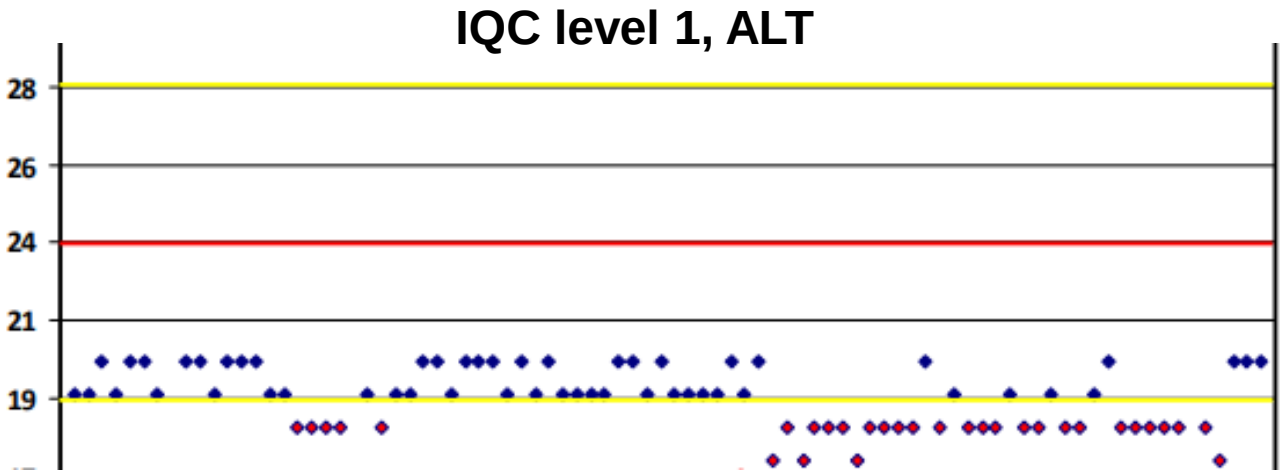
Why is an unbiased target value for IQC-I materials important?

Chemistry Systems				LEVEL 1		LEVEL 2		LEVEL 3	
				Mean	Range	Mean	Range	Mean	Range
ANALYTES			SI UNITS						
Gamma Glutamyltransferase IFCC	{4T00}	{4T96}	U/L	28.1	22.5 - 33.7	86.4	69.1 - 104	165	132 - 198
Gentamicin	{1E11}	{8P55}	µmol/L	3.66	2.93 - 4.39	9.60	7.68 - 11.5	15.7	12.6 - 18.8
Glucose	{3L82}	{7P55}	mmol/L	■	■	6.91	5.52 - 8.29	16.4	13.1 - 19.6
Haptoglobin	{9D91}	{9P59}	g/L	0.716	0.573 - 0.859	1.05	0.842 - 1.26	1.46	1.17 - 1.75
sTfR (Soluble Transferrin Receptor)	■	{6R74}	mg/L	■	■	■	■	■	■

TARGET VALUES not declared because dispersion of results from replicate analysis was too high

IQC COMPONENT I

Why is an unbiased target value for IQC-I materials important?



IS OUR SISTEM BIASED?!

IQC COMPONENT I

Why is an unbiased target value for IQC-I materials important?

CIRME
Centre for Metrological Traceability in Laboratory Medicine

To investigate the persistent systematic misalignment of ALT measuring system, we performed a **correlation between the commercial system and the IFCC reference procedure**

BIAS ESTIMATION

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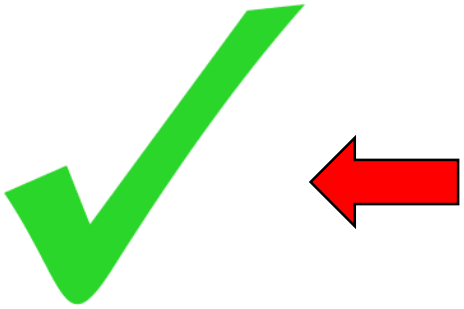
Side note: bias estimation is not part of IQC and needs a dedicated experimental protocol (i.e. CLSI EP09)

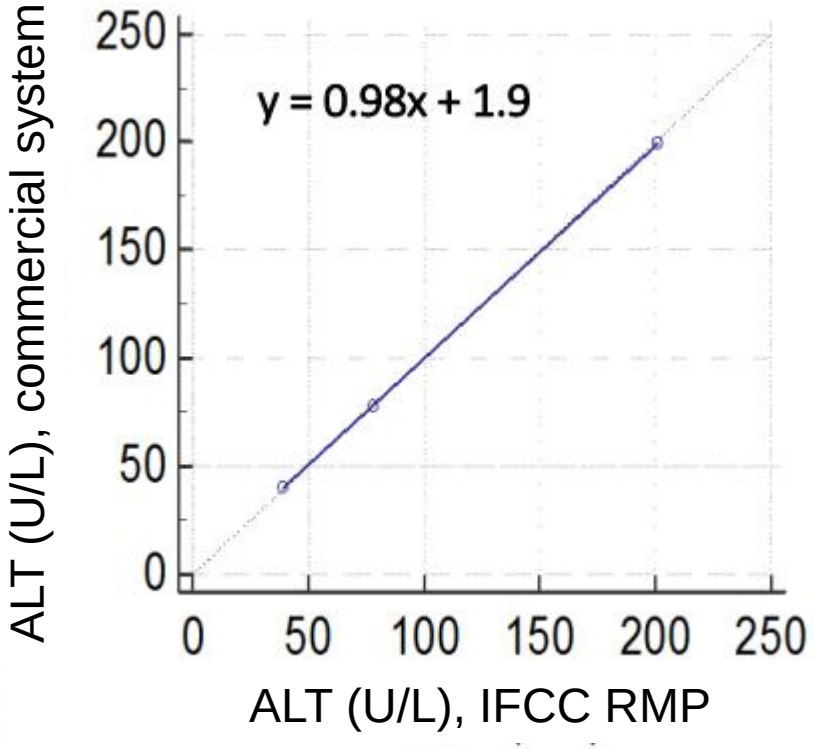
IQC COMPONENT I

Why is an unbiased target value for IQC-I materials important?



TRACEABILITY CONFIRMED!

Target value of IQC-I material is biased!



IQC COMPONENT I

Why are appropriate IQC-I acceptability ranges important?

The acceptability range defines the allowed tolerance of value deviation from the target

It must guarantee the suitable application of test results in clinical conditions.

The acceptability range provided by manufacturers is usually based on the statistical dispersion of data obtained by *n* laboratories (usually 20% of the mean value) with **no relationship with clinically suitable APS**

Values are provided only as guidelines, each laboratory should establish its own statistical limits. Laboratory means may vary from the values listed during the shelf life of the control. [redacted] monitors the values over the shelf life of the control and provides update(s) at www.[redacted].com or contact your local [redacted] customer service representative.

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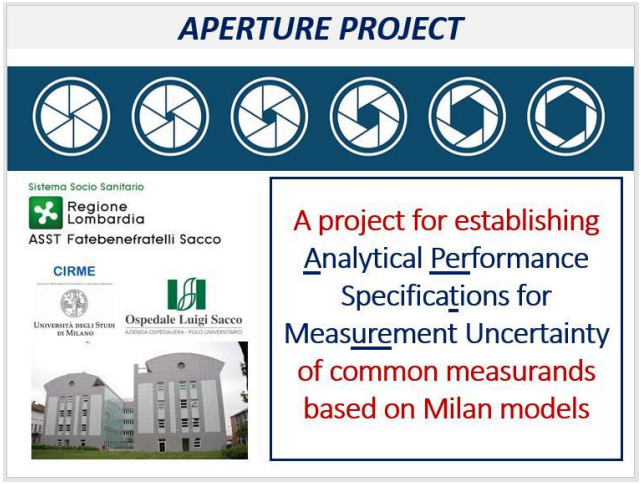
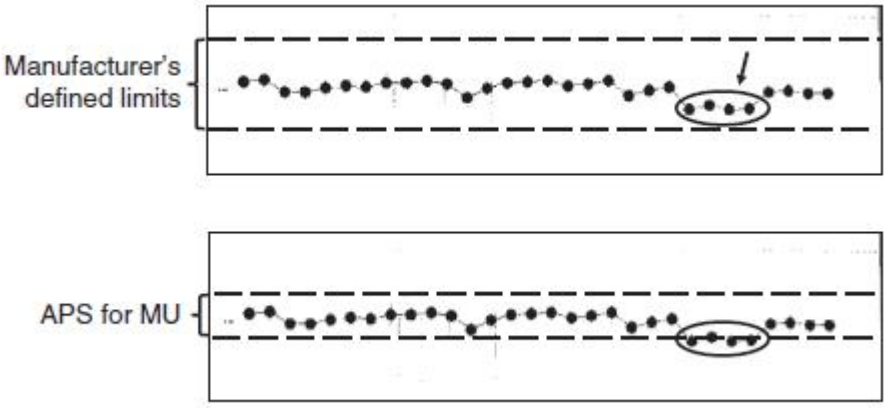
IQC COMPONENT I

Why are appropriate IQC-I acceptability ranges important?

In order for ICQ-I results to guarantee the effective surveillance of traceability of the measuring system and, more importantly, assure the suitable application of test results in clinical conditions the acceptability range for IQC-I results should correspond to APS for MU derived according to the appropriate model and it should be set based on unbiased target values



Enzymatic assay for HbA_{1c}



Clin Chem Lab Med 2021; 59(2): 291–300

IQC COMPONENT I

How do we interpret IQC-I results appropriately?

TRADITIONAL APPROACH: combination of multiple interpretative statistical rules based on different multiples of SD from the QC mean

> *"Everything should be made as simple as possible, but not simpler."*
>
> *Albert Einstein*

1

MACROEVALUATION

2

LONGITUDINAL EVALUATION

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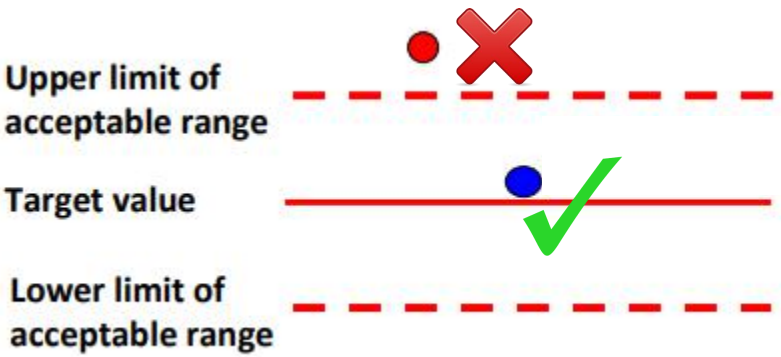
IQC COMPONENT I

1

MACROEVALUATION

Check if **a single control point** falls within the defined **ACCEPTABILITY RANGE**



IMMEDIATE ACTION!!
before results in the affected analytical run are released

Macroevaluation, if used by itself, is **not sensitive and precocious enough** to prevent the occurrence of poor quality results on clinical samples!

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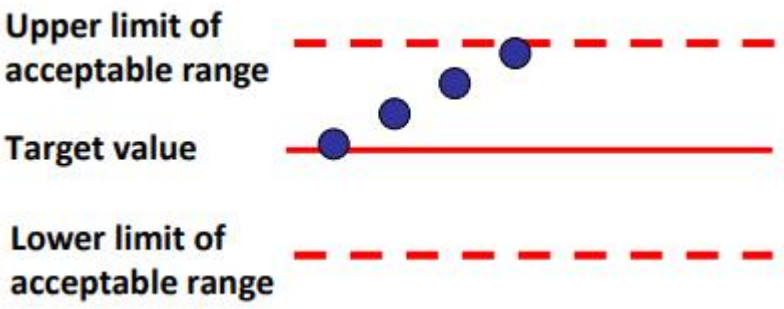
IQC COMPONENT I

2

LONGITUDINAL EVALUATION

If measurements are performed in batches → Before and at the end of each analytical run

If measurements are performed continuously h24 → Every 8 hours



Check the **TEMPORAL TREND** of **consecutive** control points in order to precociously identify potential problems

CHECK for SIGNIFICANT TRENDS
even if the macroevaluation shows that single IQC points are still within the acceptability range

EVALUATE INFLUENCE OF TREND ON u_{Rw}
as gradual or sudden changes in the alignment of the measuring system may be responsible of an unacceptable u_{Rw}

IQC COMPONENT II

WHAT IS MEASUREMENT UNCERTAINTY?

Parameter characterizing the dispersion of the quantity values being attributed to a measurand

$$\text{Result} = x \pm u$$

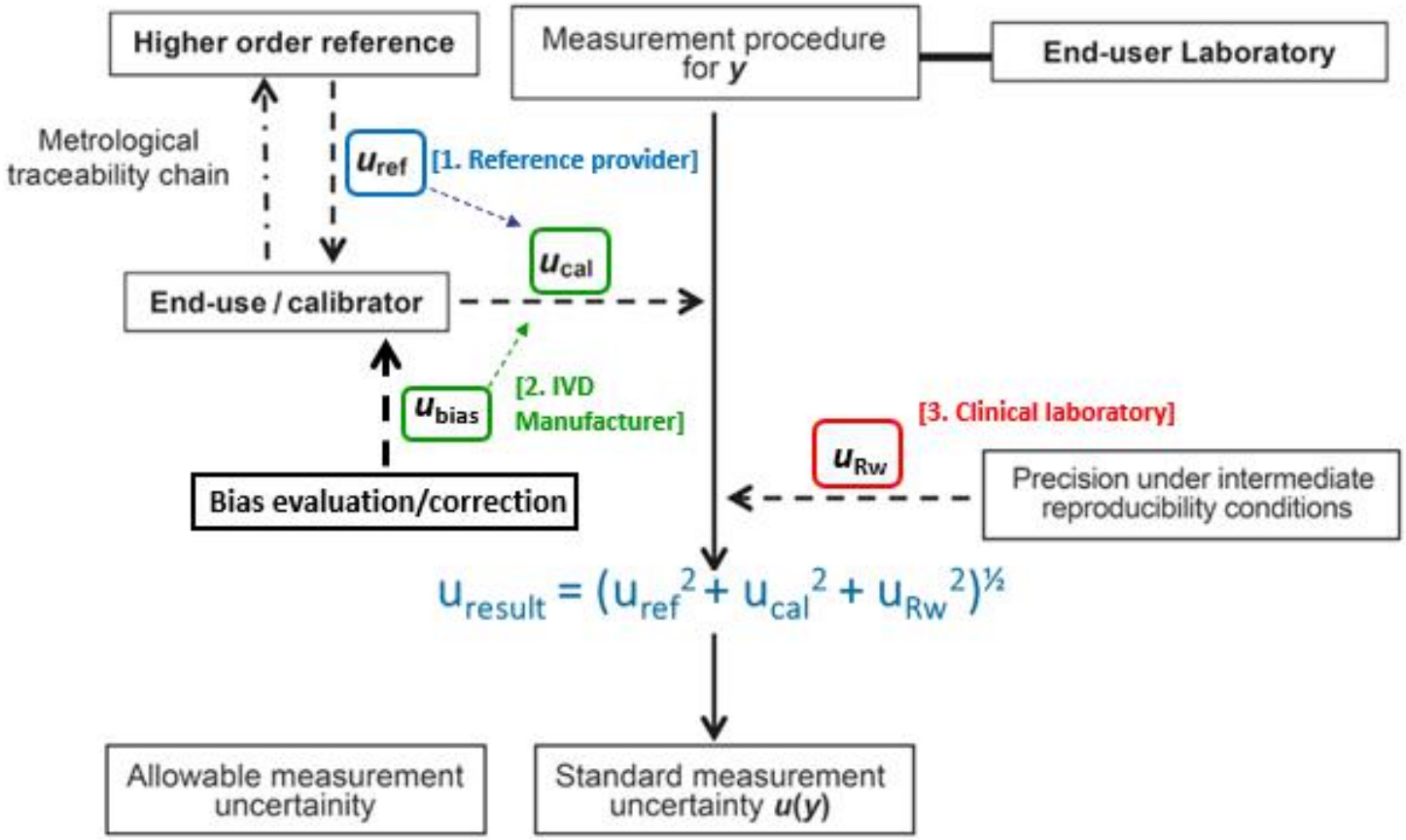
quantity value — measurement uncertainty

The value of the measurand is assumed to lie within the interval $x - u$ to $x + u$ units, with a stated level of confidence.

[International Vocabulary of Metrology Basic and general concepts and associated terms (VIM). 3rd ed. 2012]

IQC COMPONENT II

Estimating MU by «top-down» approach



ISO/TS 20914:2019
MEDICAL LABORATORIES -- PRACTICAL GUIDANCE FOR THE ESTIMATION OF MEASUREMENT UNCERTAINTY

IQC COMPONENT II

WHAT IS RANDOM UNCERTAINTY (u_{Rw})?

Portion of measurement uncertainty accounting for random sources of error

It gives information about the stability of the measuring system over time and its variability when employed by an individual laboratory

IQC COMPONENT II

MAIN SOURCES OF u_{Rw}

Analytical system

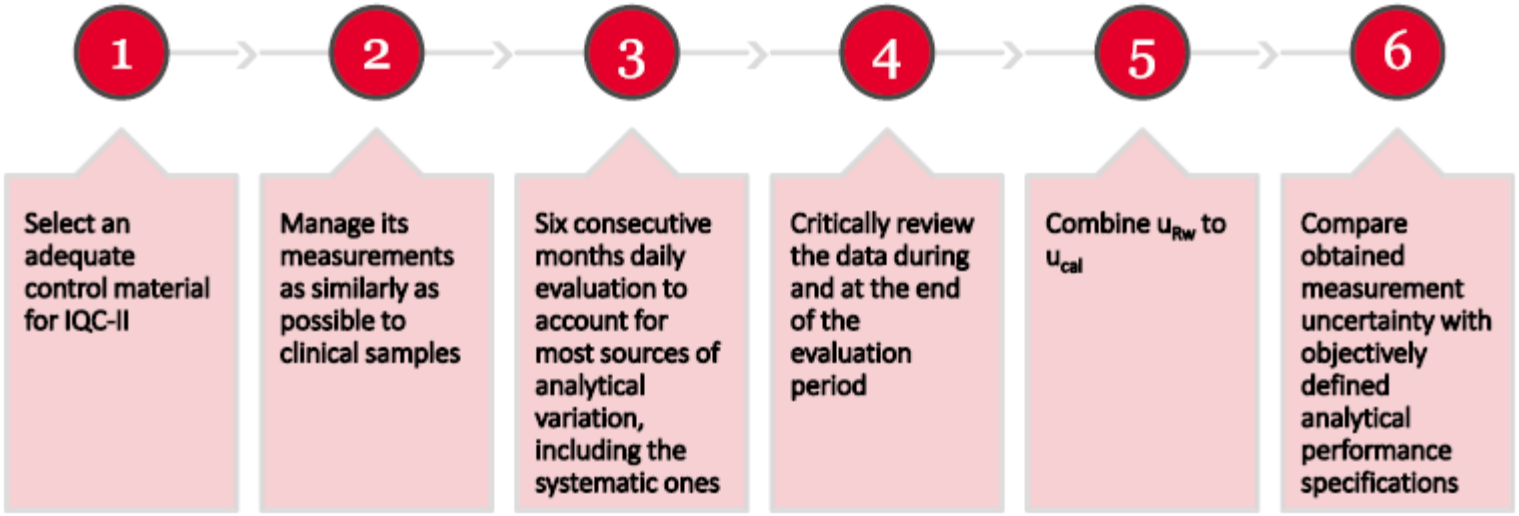
- Reagent lot variability
- Calibrator lot variability
- Reagent/Calibration stability
- Measuring equipment

Individual lab

- Environmental conditions
- Different operators
- Instrument maintenance
- Material preparation

IQC COMPONENT II

HOW TO CORRECTLY ESTIMATE u_{Rw}



Clin Chem Lab Med 2023; 61(5): 759–768

IQC COMPONENT II

1

HOW TO SELECT IQC-II MATERIAL

Select an adequate control material for IQC-II

Different from that used for IQC-I

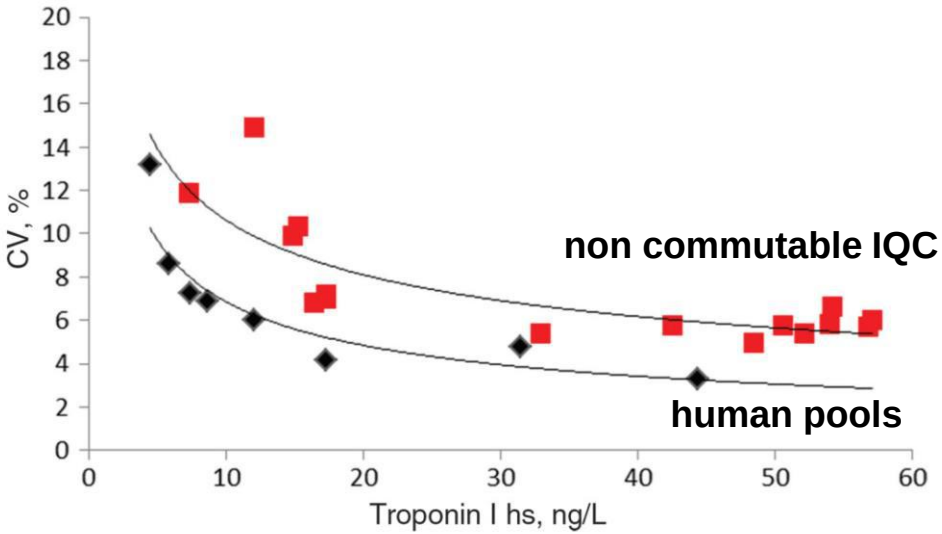
"medical laboratories should (…) establish and maintain routines for estimating and minimizing them separately"

Oosterhuis WP et al. Clin Chem Lab Med 2018;56:209–19

Components I & II should be independent

Commutable

results obtained on non-commutable materials may not reflect performances achieved by the same IVD-MD on clinical samples in terms of u_{Rw}



Hage-Sleiman et al. Clin Chem Lab Med 2019;57:e49

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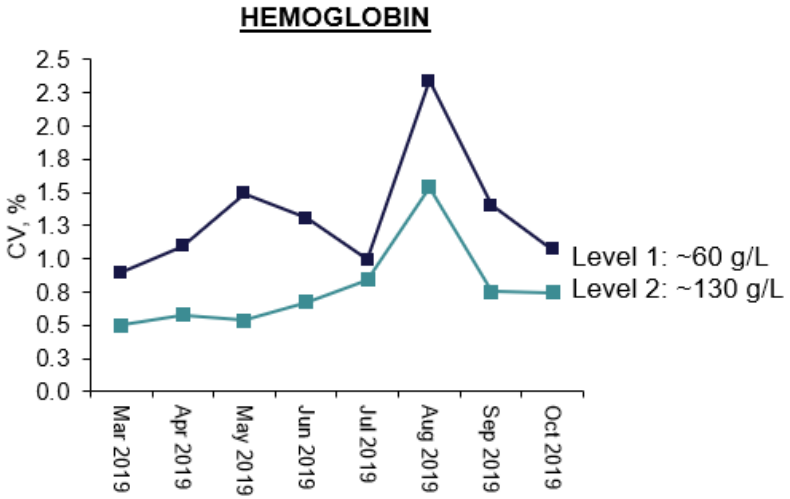
IQC COMPONENT II

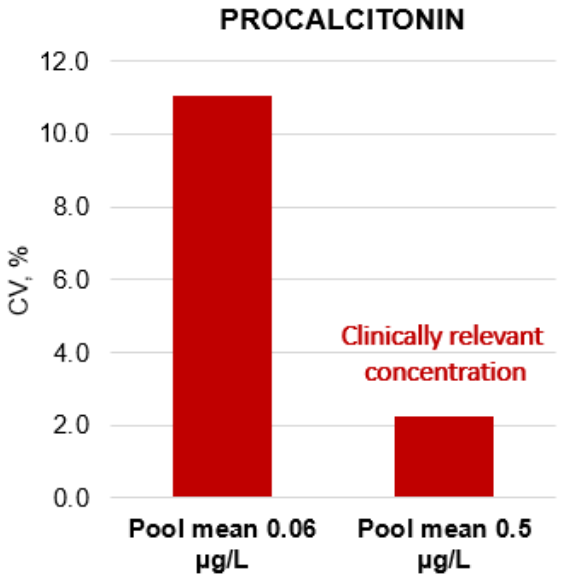
1

Select an adequate control material for IQC-II

Analyte concentrations should be close to clinical decision thresholds

u_{Rw} often varies with analyte concentration





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IQC COMPONENT II

2

Manage its measurements as similarly as possible to clinical samples

The ultimate goal of IQC-II is to estimate measurement uncertainty of patient results

CONTROL MATERIAL SHOULD BE HANDELED AS CLOSELY AS POSSIBLE AS CLINICAL SAMPLES

IQC COMPONENT II

3

Six consecutive months daily evaluation to account for most sources of analytical variation, including the systematic ones

Measurements performed under **intermediate precision conditions**:

ISO 20914:2019 → condition of measurement, out of a set of conditions that includes the same measurement procedure, same location, and replicate measurements on the same or similar objects over an extended period of time but may include other conditions involving changes.
The changes can include new calibrations, calibrators, operators, and various platforms.

IQC COMPONENT II

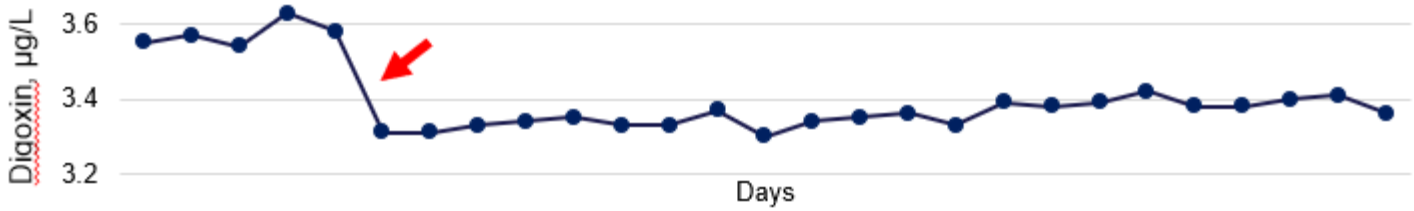
4

Critically review the data during and at the end of the evaluation period

EXPLAINABLE OUTLIER: TO BE EXCLUDED

SHIFT DUE TO THE NEW BATCH OF CONTROL MATERIAL

SHIFT DUE TO A NEW CALIBRATION: KEEP ALL RESULTS IN THE CALCULATION



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IQC COMPONENT II

5

Combine u_{Rw} to u_{cal}

HOW TO CALCULATE u_{Rw}

$$u_{Rw} = CV = \frac{SD}{Mean} x\ 100$$

SD = standard deviation of replicates
Mean = mean of replicates

If more than one IQC-II material batch/lot is used in the evaluation period:

$$u_{RW} = [(n_1 * u_1^2 + n_2 * u_2^2)/(n_1 + n_2)]^{1/2}$$

Where IQC Lot 1 = u_1, IQC Lot 2 = u_2, # days IQC Lot 1 = n_1, # days IQC Lot 2 = n_2

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HOW TO CALCULATE MU

ISO 15189:2022 → medical laboratories should determine MU for each measurement procedure used to report measured quantity values on patients' samples.

$$u_{result} = (u_{cal}^2 + u_{Rw}^2)^{½}$$

ASSUMPTION: bias should be appropriately corrected by IVD manufacturer before marketing

All commercial calibrators have an uncertainty derived from the value assignment procedure which contributes to the overall uncertainty of measurement results.

$$u_{cal} = (u_{ref}^2 + u_{ass\ value}^2)^{½}$$

IQC COMPONENT II

6

Compare obtained measurement uncertainty with objectively defined analytical performance specifications

APERTURE PROJECT

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CIRME
Università degli Studi di Milano
Ospedale Luigi Sacco
Azienda Ospedaliera - Polo Universitario

A project for establishing Analytical Performance Specifications for Measurement Uncertainty of common measurands based on Milan models

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IQC COMPONENT II

WHAT CAN A CLINICAL LAB DO IF MU > APS?

- Check variables that may influence $u_{Rw,}$ both related to the measuring system, such as frequency of calibrations, calibrator & reagent lot changes, instrumental maintenance procedures, ecc. AND related to the laboratory such as environmental factors or differences in operator usage

› Ann Clin Biochem. 2024 Mar;61(2):154-155. doi: 10.1177/00045632231216598. Epub 2023 Nov 18.

Closed analyser lids do not reduce the measurement uncertainty of serum total carbon dioxide

Platforms	No. of determinations over a 6-month period	Mean tCO_2 concentration (mmol/L)	u_{Rw} (%)
Architect c16000	121	29.3	2.28
Alinity c08	133	32.8	4.16
Alinity c09	125	32.4	3.94
Alinity cic1	139	30.6	4.82
Alinity cic2	138	30.1	4.51

IQC COMPONENT II

WHAT CAN A CLINICAL LAB DO IF MU > APS?

- Select a measuring system traceable to a metrological chain which carries an overall lower uncertainty

Metrological traceability and uncertainty information derived from calibrator package inserts of commercial systems measuring serum creatinine marketed by four in vitro diagnostics companies.

Company	Platform	Principle of commercial method	Calibrator	Declared standard uncertainty[a]	Higher order reference employed		Type of traceability chain used[b]	Combined standard uncertainty associated with the used chain[c]
					Method	Material		
Abbott	Architect	Enzymatic	Multigent clin chem calibrator	1.48%	IDMS	NIST SRM 967	A	2.12%–2.79%[d]
		ND	Multiconstituent calibrator	2.7%	IDMS	NIST SRM 967	A	2.12%–2.79%[d]
Beckman	AU	Enzymatic	System calibrator	ND	ND	NIST SRM 967	A	2.12%–2.79%[d]
		Alkaline picrate	System calibrator	ND	IDMS	NIST SRM 967	A	2.12%–2.79%[d]
		Uncompensated alkaline picrate	System calibrator	ND	ND	NIST SRM 909b L2	B	1.51%
	Synchron	ND	LX aqua calibrator	ND	IDMS	NIST SRM 914a	D	1.5%[e]
Roche	Cobas c	Enzymatic	C.f.a.s.	0.91%	IDMS	ND	D	1.5%[e]
		Alkaline picrate compensated	C.f.a.s.	1.62%	IDMS	ND	D	1.5%[e]
		Alkaline picrate rate–blanked and compensated	C.f.a.s.	1.42%	IDMS	ND	D	1.5%[e]
	Integra/Cobas c111	Enzymatic	C.f.a.s	1.06%	IDMS	ND	D	1.5%[e]
	Integra400/Cobas c111	Alkaline picrate compensated	C.f.a.s	0.30%	IDMS	ND	D	1.5%[e]
	Integra800	Alkaline picrate compensated	C.f.a.s	0.72%	IDMS	ND	D	1.5%[e]
	Modular	Enzymatic	C.f.a.s	0.91%	IDMS	ND	D	1.5%[e]
		Alkaline picrate compensated	C.f.a.s	1.38%	IDMS	ND	D	1.5%[e]
		Alkaline picrate rate-blanked and compensated	C.f.a.s	0.79%	IDMS	ND	D	1.5%[e]
Siemens	Dimension Vista	Enzymatic	ECREA calibrator A	5.08%[f]	ND	NIST SRM 914a	C	NA
			ECREA calibrator B	3.16%[f]	ND	NIST SRM 914a	C	NA
		Alkaline picrate	Chemistry calibrator	1.6%	GC-IDMS	NIST SRM 914a	D	1.5%[e]
	Advia	Enzymatic	Chemistry calibrator	0.45%	IDMS	NIST SRM 914a NIST SRM 967	A	2.12%–2.79%[d]
		Alkaline picrate rate-blanked and compensated	Chemistry calibrator	1.6%	IDMS	NIST SRM 967	A	2.12%–2.79%[d]

Clin Chem Lab Med 2015; 53(6): 905–912

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IQC COMPONENT II

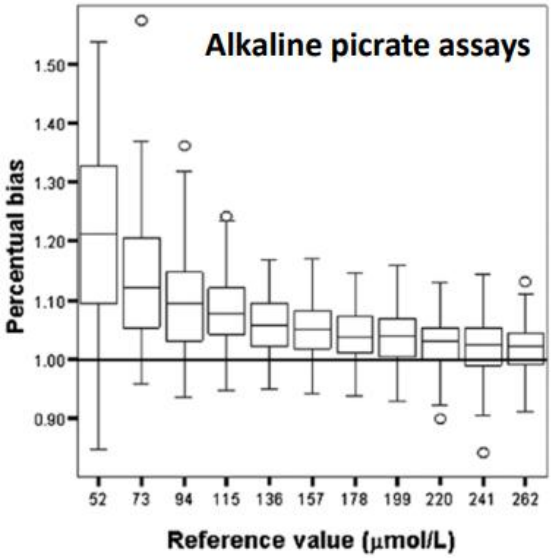
WHAT CAN A CLINICAL LAB DO IF MU > APS?

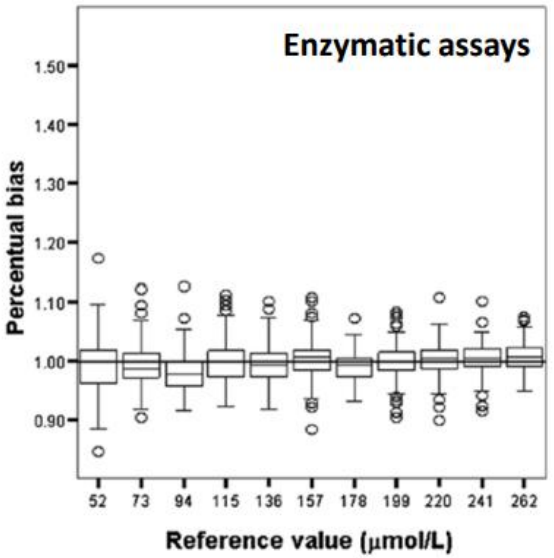
- Abandon non-selective methods and move to IVD-MDs displaying proper selectivity, which is one of the indispensable prerequisites for the correct implementation of metrological traceability

Selectivity:

"Property of a measuring system, used with a measurement procedure, whereby it provides measured quantity values for one or more measurands such that the values of each measurand are independent of other measurands or other quantities in the phenomenon, body, or substance being investigated."

International Vocabulary of Metrology





Drion *et al. BMC Nephrology* 2012, **13**:133

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"ALT IVD-MDs without P-5'-P activation are often unable to fulfil quality specifications when ALT results are compared to RMP. Unfortunately, almost all IVD manufacturers still market IVD-MDs with or without the addition of P-5'-P and declare that both are traceable to the IFCC RMP."

Table 1: Recommended priority tasks, together with the relevant responsibilities, that should be implemented to obtain harmonization of alanine aminotransferase (ALT) measurements in medical laboratories.

Task	Responsibility
Transfer trueness from the 2002 IFCC reference measurement procedure to commercial calibrators according to ISO 17511:2020 standard	IVD manufacturers
If a strategy of IVD-MD calibrator value assignment with a reference material is selected, preliminarily assess its commutability with the given IVD-MD	IVD manufacturers Reference material providers International standardization bodies
In transferring trueness to IVD-MD calibrator, check if significant bias is present and, in case, correct it	IVD manufacturers
Make explicit the full information about the implementation of metrological traceability of commercial IVD-MD for measuring ALT	IVD manufacturers
Choose only selective IVD-MD for ALT measurements incorporating pyridoxal-5-phosphate	Laboratory professionals
Fulfil the analytical performance specifications for maximum allowable standard measurement uncertainty of ALT measurements, i.e., 4.65 % (desirable quality) and 6.98 % (minimum quality level), respectively, at the level of clinical samples	Reference material providers IVD manufacturers Medical laboratories
Provide and participate in suitable EQAS	EQAS providers Medical laboratories IVD manufacturers

IVD-MD, *in vitro* diagnostic medical device; EQAS, external quality assessment schemes.

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Clin Chem Lab Med 2024; 62(2): 249–252

IQC COMPONENT II

WHAT CAN A CLINICAL LAB DO IF MU > APS?

ASK MANUFACTURERS TO IMPROVE THEIR SYSTEMS!

USING IQC DATA: EXAMPLE

Manufacturer and platform	Reagent name (code)	Procedure principle	Calibrator name (code)	Stated traceability	Standard MU of reference material (u_{ref}), %	Procedure for transferring trueness to commercial calibrator	Standard MU of calibrator value (u_{cal}), %	Intermediate reproducibility data			Combined standard MU on clinical samples[b], %
								Number of measurements over a 6-month period	Mean TPU, mg/L[a]	Standard MU accounting for random sources (u_{Rw}), %	
Abbott diagnostics architect c16000	Urine/CSF protein (7D79)	Turbidimetry with benzethonium chloride	Urine/CSF protein (08P71)	NIST SRM 927c (bovine serum albumin, 7 % solution)	0.52	Biuret reference procedure for serum total protein	3.33[c]	205	276.7	3.96	5.20
Abbott diagnostics alinity c	Urine/CSF protein (07P59)	Turbidimetry with benzethonium chloride	Urine/CSF protein (08P71)	NIST SRM 927c (bovine serum albumin, 7 % solution)	0.52	Biuret reference procedure for serum total protein	3.33[c]	158	253.9	3.65	4.97
Beckman Coulter AU680	Urinary/CSF protein (OSR6170)	Pyrogallol red molybdate	Urinary/CSF protein (OSR6170)	Reagent-grade human serum albumin	NA	Gravimetrically prepared primary internal standard	1.80[d]	159	312.2	4.74	5.07[e]
Roche diagnostics Cobas c501	Total protein urine/CSF Gen. 3 (08058679190)	Turbidimetry with benzethonium chloride	C.f.a.s. PUC (03121305122)	NIST SRM 927c (bovine serum albumin, 7 % solution)	0.52	Primary standard material "traceable to NIST"	1.33[f]	134	203.6	4.89	5.09

TOTAL URINE PROTEIN

ALLOCATION TO MODEL 3 (State of the art):

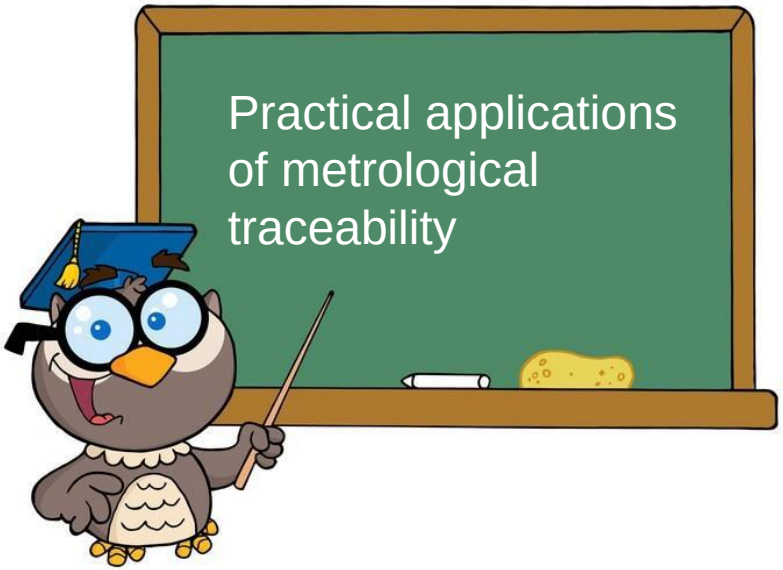
- No strict homeostatic control ✓
- (temporarily) used for measurands with defined diagnostic role but still waiting for outcome-based APS ✓

Definition of u_{result} APS based on Model 3:

Desirable = 4.97%
Minimum = 7.46%

Clin Chem Lab Med 2024; 62(8): e175–e177

CONCLUSIONS



The practical application of metrological traceability concepts is difficult but not impossible.

In order to improve, **relevant education** and appropriate training **of all involved stakeholders** are essential to obtain the expected benefits in terms of standardization.

IVD manufacturers should:

- Guarantee **correct traceability** of their marketed measuring system;
- Provide a **IQC material as a part of the system**, suitable for traceability verification and alignment surveillance by end-users in daily practice (IQC component I)
- Provide **unbiased target values** for IQC-I materials
- Provide **adequate acceptability ranges** for IQC-I materials corresponding to APS for suitable MU on clinical samples.

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CONCLUSIONS

Medical laboratories should:

- **Improve the IQC process** by implementing a program designed to give information about metrological traceability and MU of employed IVD-MD (as described in this presentation)
- **Improve IQC judging criteria** to establish a direct link between performance, estimated as MU, and APS, defined according to Milan models
- **Apply prompt corrective actions** (by also involving the IVD-MD manufacturer if necessary) if performances do not fulfill judging criteria and are at risk of jeopardizing the clinical validity of test results

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