

IUPAC Internal Quality Control Protocol and method verification using reference materials and proficiency testing



Franz Ulberth

European Commission
Joint Research Centre
Institute for Reference Materials and Measurements

<http://www.irmm.jrc.be>
<http://ec.europa.eu/dgs/jrc/index.cfm>

- millions of measurements are performed every year to implement European legislation
- important decisions are taken based on those measurements
- need for harmonized implementation of policies



The three pillars

- **Metrology**

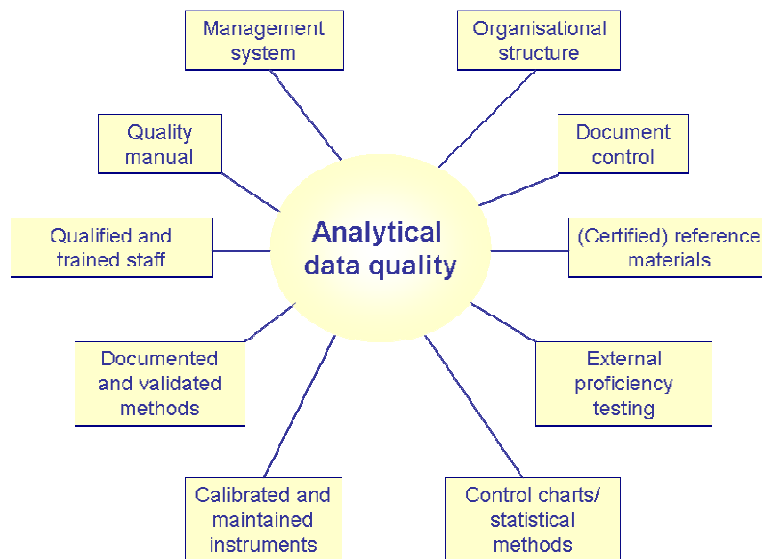
- Metre convention
- National metrology institutes

- Accreditation
- National accreditation bodies



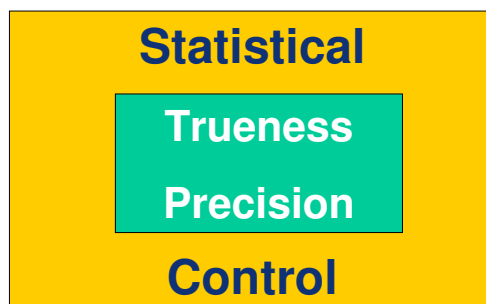
- **Standardisation**

- (Inter)national standardisation organisation
- Professional/trade associations



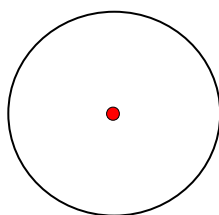
- **Set of procedures undertaken by laboratory staff for the continuous monitoring of operation and the results of measurements in order to decide whether results are reliable enough to be released.**

Pure & Appl. Chem. 67 (1995) 649

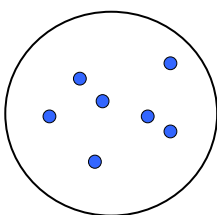


Statistical control \approx Stability of operation

Error concepts in analytical chemistry



Ideal



Reality

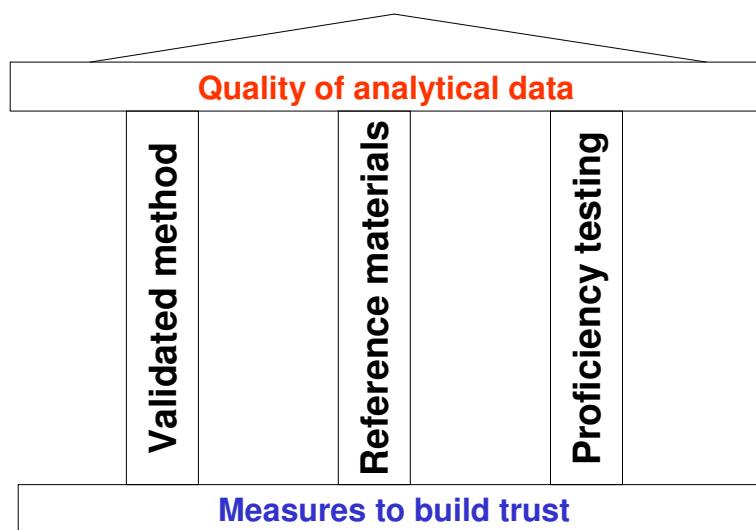
Repeatability
Reproducibility
Trueness

Method

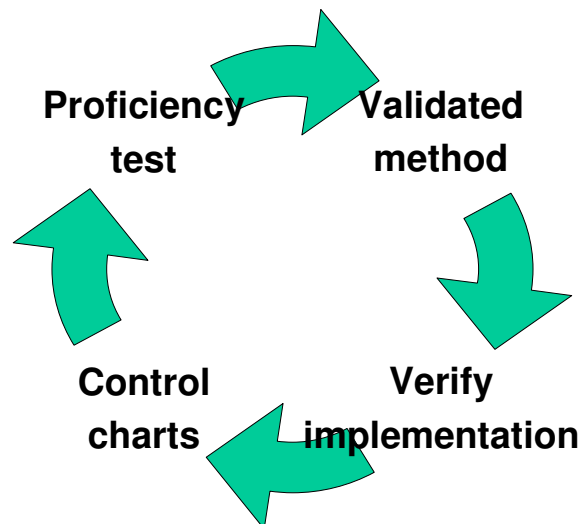
Homogeneity
Stability

Material

Quality assured analytical data



- Easily available
- Complete documentation
- Proven performance
- Acceptance
- Consensus
- Market driven



- **Should be representative:**
 - of the test materials under consideration with respect to matrix composition,
 - of the state of physical preparation
 - of the concentration range of the analyte(s)
- **Subjected to same measurement procedure as the test items**
 - duplicates
 - randomized

- **Material, sufficiently homogeneous and stable with reference to specified properties, which has been established to be fit for its intended use in measurement or in examination of nominal properties.**
- **NOTE Reference materials with or without assigned quantity values can be used for measurement precision control whereas only reference materials with assigned quantity values can be used for calibration or measurement trueness control.**

Performance verification of standardised methods (I)

EURACHEM Guide: The Fitness for Purpose of Analytical Methods: A Laboratory Guide to Method Validation and Related Topics

- It is often assumed that standard methods can be used straight off the shelf and the published performance data achieved straight away by whoever uses the method. This is not a safe assumption.
- Competence might be established in terms of the analyst's ability to achieve the levels of performance stated in the method, such as repeatability, limit of detection, etc.

Performance verification of standardised methods (II)

IUPAC Harmonized Guidelines for Single Laboratory Validation of Methods of Analysis

- A laboratory using a collaboratively studied method, which has been found to be fit for the intended purpose, needs only to demonstrate that it can achieve the performance characteristics stated in the method
- The laboratory should undertake precision studies, bias studies (including matrix variation studies), and possibly linearity studies



http://www.aoac.org/alacc_guide_2008.pdf

PURPOSE

The purpose of the guide is to define the activities that are required to fulfill method verification based on analytical method performance characteristics.

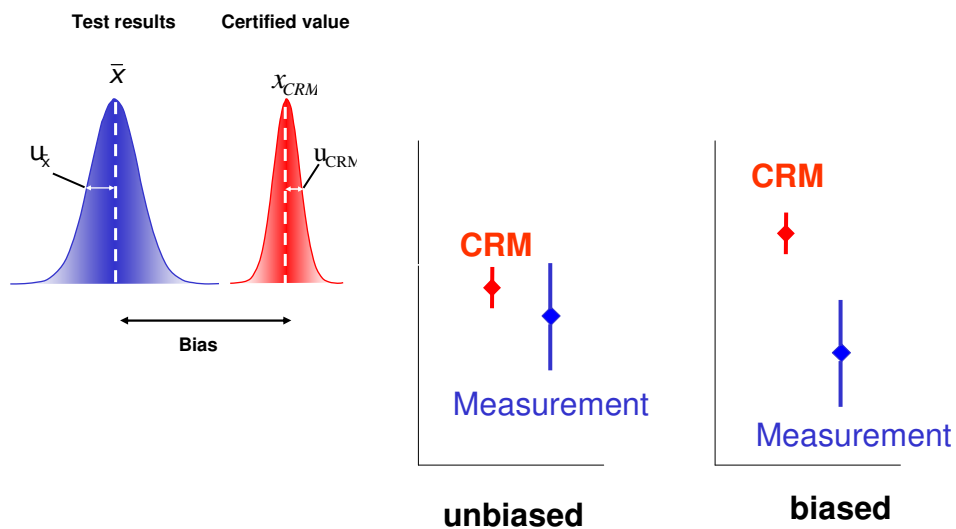
ISO 17025:2005 section 5.4.2 states:

"...The laboratory shall confirm that it can properly operate standard methods before introducing the tests or calibrations. If the standard method changes, the confirmation shall be repeated."

- The results of a collaborative study yield performance indicators (s_R , s_P) and, in some circumstances, a method bias estimate, which form a “specification” for the method performance.
- In adopting the method for its specified purpose, a laboratory is normally expected to demonstrate that it is meeting this “specification.”
- In most cases, this is achieved by studies intended to verify control of precision and bias

- To demonstrate that repeatability is consistent with the repeatability standard deviation obtained in the course of the collaborative exercise
 - replicate analysis of one or more suitable test materials, to obtain a repeatability standard deviation of s_r
 - compare, using an F -test if necessary, with the repeatability standard deviation s_r obtained in the collaborative study.

	AOAC 999.07				Verification study				F	Fcrit (95 %)
	Mean [ng/g]	# Labs	sr	RSDr	Mean [ng/g]	# Repl.	sr	RSDr		
Spiked	0.9	15	0.09	10	0.85	5	0.02	2.5	0.233	4.56
Spiked	3.6	13	0.11	3	3.34	5	0.08	2.5	0.764	4.86
Contaminated	0.8	15	0.05	6	0.82	4	0.01	1.0	0.160	4.89
Contaminated	1.5	14	0.10	7						
Contaminated	3.4	14	0.13	4	3.16	4	0.09	2.8	0.669	5.04



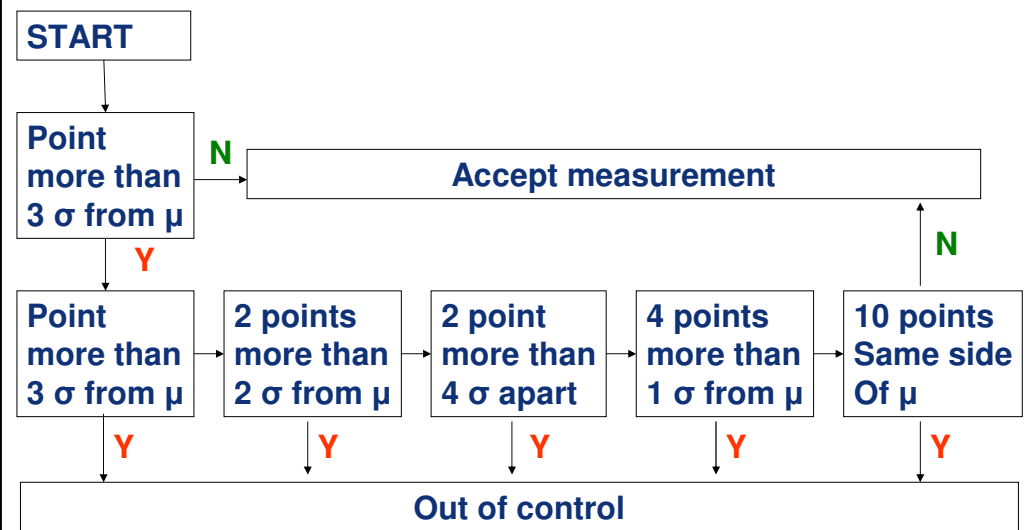
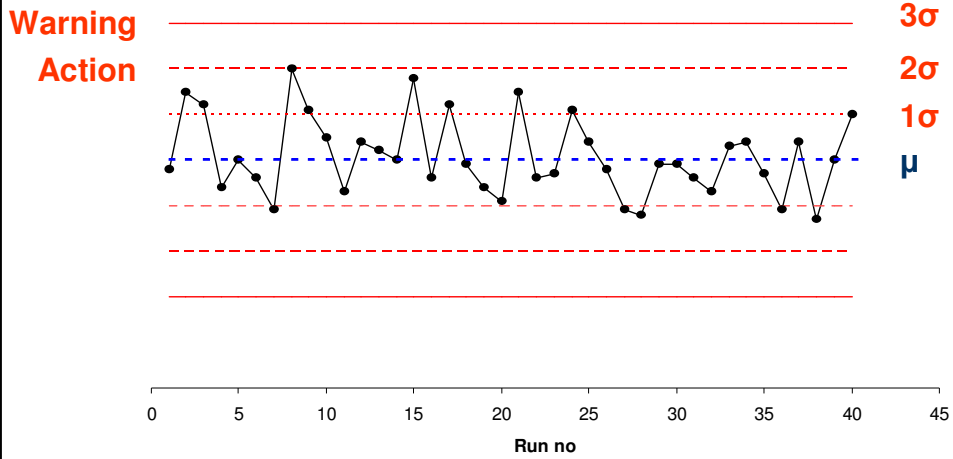
- To demonstrate that bias of the method is under control
 - perform replicate measurements on a reference material under repeatability conditions
 - calculate standard deviation of measurements (s_w)
 - form an estimate Δ (= laboratory mean – reference value) of bias on this material

$$|\Delta| < 2\sqrt{(s_R^2 - s_r^2 + s_w^2/n)}$$

	AOAC 999.07				Verification study				
	Mean [ng/g]	# Labs	sr	sR	Mean [ng/g]	# Repl.	sr	Δ	$2\sigma_D$
Contaminated	0.8	15	0.05	0.26	0.82	4	0.01	0.02	0.51
Contaminated	3.4	14	0.13	0.65	3.16	4	0.09	0.24	1.28

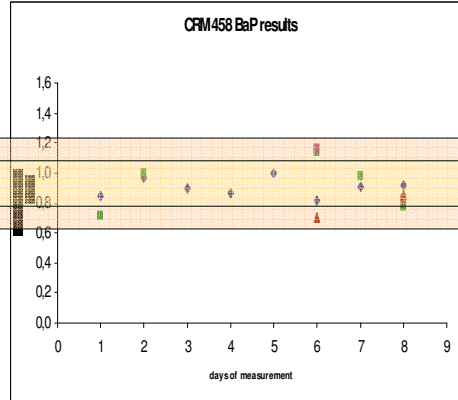
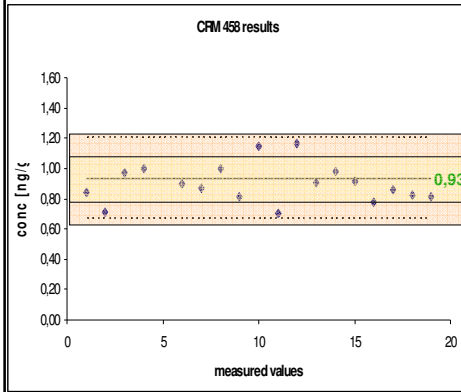
- Selection of suitable test material(s)
- Selection of suitable reference standards
- Deviations from collaborative study testing conditions with respect to sampling, sample pre-treatment, and matrix effects
- Number of experiments to be carried out (e.g. calibration, precision and bias study)
- Statistical data treatment
- Regulatory aspects





BCR-458 (PAHs in coconut oil) measured on 8 different days over ~1 year

n=18



%RSD*2

%RSD*1

%RSD*2

Mean=0.90 ng/g

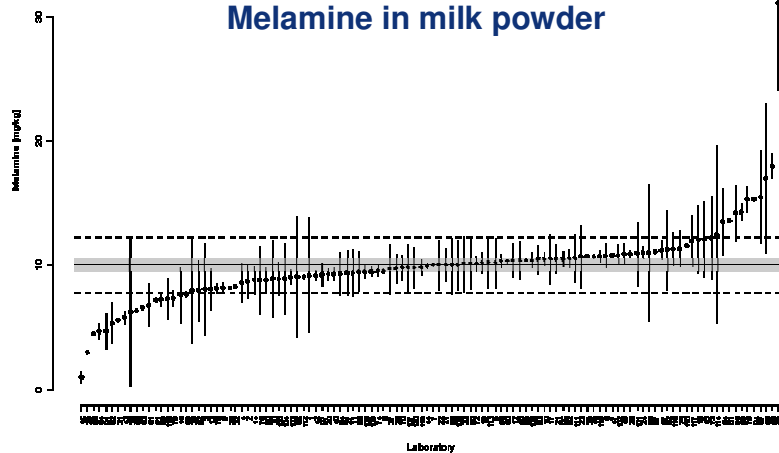
SD=0.13

%RSD=14,1%

CRM certified value: 0.93±0.1 ng/g
(expanded uncertainty, k=2)

$x_c = 10.01 \text{ mg/kg}$
 $U(x_c) = 0.65 \text{ mg/kg (k=2)}$
 $2 \times s(x_c) = 1.12 \text{ mg/kg}$

Melamine in milk powder



- External quality control measure
- Laboratory analyses unknown 'real-life' sample under business-as-usual conditions
- Monitors ability of a laboratory to deliver fit-for-purpose result
- Scheme provider calculates scores that reflect lab performance

$$z = \frac{(x - x_a)}{\sigma_p}$$

Acceptable if $z < |2|$
Unacceptable if $z > |3|$

- basis for self-help for each participant

- Quality assurance requires integrated system
- Importation of validated methods requires verification
- Internal quality control assures stability of performance
- External quality assessment flags problems if present

www.jrc.cec.eu.int
www.jrc.irmm.be

franz.ulberth@ec.europa.eu