EUROPEAN COMMISSION
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Institute for Reference Materials and Measurement

TrainMiC - Training in Metrology in Chemistry

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TrainMiC
Training in Metrology in Chemistry

Report EUR 20841 EN

The mission of IRMM is to promote a common European measurement system in support of EU policies, especially health and consumer protection, environment, agriculture, internal market and industrial standards.

European Commission
Directorate-General Joint Research Centre
Institute for Reference Materials and Measurements

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TrainMiC
Training in Metrology in Chemistry

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From February 2001 to August 2003:

17 events
in 8 countries =
794 participants

Abstract

A common understanding of issues related to measurement science applied to chemistry is essential among European member states and acceding-candidate countries. An education platform was therefore created to respond to this challenge: **TrainMiC**, Training in Metrology in Chemistry.

After a brief presentation of TrainMiC and an overview of TrainMiC events, this report provides the complete set of the training material. The seven modules are included in the Appendix.

Table of Contents

1. What is TrainMiC?

Today's society relies on a proper measurement infrastructure, e.g. to realise the EU internal market and enable international trade, to implement regulations to, guarantee consumer protection, to support scientific research...

Key players in such an infrastructure are measurement service providers (national metrology institutes, national and community reference laboratories, inspection and control laboratories…), national accreditation bodies, and organisations responsible for education & training.

IRMM is the metrology institute of the European Commission. The mission of IRMM is to promote a common European measurement system in support of European Union policies. IRMM launched in 2001 its Metrology in Chemistry support programme for EU candidate countries in support of enlargement. One of the initiatives of the support programme is TrainMiC. TrainMiC has been set up as a training platform for people out of all types of organisations. Via the TrainMiC platform, a set of training modules has been constructed that **provides understanding in basic measurement matters, that apply across sectors** (food, environment, clinical…). **It offers interpretation of existing documents and gives guidance by making available concrete examples. The training material strives towards a congruent and up-to-date view** (e.g. regarding uncertainty, traceability of measurements).

The target audience for such courses is:

- Measurement practitioners from laboratories
- Technical assessors involved in accreditation
- End-users of measurement data (e.g. from public bodies, enforcement agencies ...)

The training courses are organised by the local partners, such as NMIs, universities or accreditation bodies, in collaboration with the IRMM.

Why should I participate in TrainMiC?

Better quality measurement results can be obtained if the people producing these results have insight into basic measurement issues. This is why the ISO/IEC 17025 requires the laboratory to address measurement traceability, uncertainty and validation. The course will help you to do this.

Who should attend TrainMiC courses?

Laboratory managers, analysts or anyone responsible for the quality of the analytical results.

What do I benefit from attending a TrainMiC course?

During the training course you will be taught how to:

- Validate measurement procedures;
- Establish and demonstrate traceability of measurement results;
- Estimate measurement uncertainty based on the Guide to the Expression of Uncertainty in Measurements (GUM) and basic statistics supporting these;
- Use properly reference materials
- Interpret the outcome of inter-laboratory comparisons.

Questions after attending a TrainMiC course?

IRMM staff is available to answer questions via the email address *trainmic@cec.eu.int* The TrainMiC web site (*www.trainmic.org*) can also act as a source of information for your questions.

2. Mission, Vision and Credo

Our Vision

We want TrainMiC to be a European high quality shareware product/process for training in generic issues related to the measurement science in chemical measurements (metrology in chemistry).

Our Values

- ✓ **Realism** — *just do what you can, it will never be perfect; the truth can only be approximated*
- ✓ **Transparancy** — *document in an open and complete way*
- ✓ **Being critical**
- ✓ **Standardised terminology** — *we use a similar terminology and practices across disciplines & sectors, based on VIM and ISO-GUM wherever possible*

Our Mission

Our purpose is *to facilitate the training about metrology in chemistry* to interested parties, such as metrology organisations, educators, decision-makers and accreditors, in order to strengthen the measurement infrastructure. Hence, the trustworthy results produced would then avoid economic or societal wastes.

Our Actions

- TrainMiC events, using approved TrainMiC trainers and course materials;
- National events with TrainMiC materials and additional lecturers and complementary modules
- Dedicated training of TrainMiC trainers

Our Strategy

TrainMiC is run in a **distributed way**, with national metrology institutes, selected academic faculties and national accreditation bodies together with their regional organisations EUROMET/EURACHEM and EA.

The TrainMiC **management board,** chaired by the IRMM, consists of the project leader, a project co-ordinator and one representative per acceding/candidate country, originating from the academia, accreditation bodies or metrology institutes. The board sets the TrainMiC policies, creates and controls the processes (e.g. the type of training courses) and the products (e.g. the course content).

Members of TrainMiC management board are called **ambassadors**. Their task it is to coordinate all TrainMiC activities at the national level and refer to the management board regarding ongoing courses, course content, new needs, etc. The list of ambassadors can be found on the TrainMiC web site (*www.trainmic.org*).

Training is performed using the **TrainMiC material** that has been reviewed, approved and edited by the board with the TrainMiC logo on each slide (cf. Appendix).

Hard copies of the authorised training material are distributed to the training participants. The TrainMiC website contains some ‘appetiser’ extracts of the course and not the complete material, as we want attendants to follow and actively participate to this interactive course.

The TrainMiC modules will be **translated**, when necessary, in local languages, under the responsibility of the ambassador.

TrainMiC trainers are proposed by the ambassador, selected and authorised by the board. The board organises training sessions for trainers.

Certificates for participation to TrainMiC courses are awarded via the TrainMiC board, stating the modules that were followed.

The **TrainMiC logo** can be used on the invitation to events, only when:
- at least one authorised TrainMiC module is presented and
- the ambassador is responsible for the scientific programme of the specific event.

Such event may contain complementary presentations addressing the needs of specific audiences, without the TrainMiC logo.

TrainMiC courses are organised at the national/regional level by a local host organisation, which is responsible for all practical arrangements (selection of participants and logistics). This organiser can request sponsoring from IRMM for this activity. Additionally, it can decide to charge a participation fee, so as to secure a self-sustaining operation.

Our major assets

- Well established contacts with the major National stakeholders, such as academia, national metrology institutes and accreditation bodies.
- Structured and coherent course material
- Experienced trainers
- Efficient national logistics and infrastructure

3. Description of the TrainMiC modules

3.1 General Introduction to Metrology in Chemistry.

Quality of chemical measurements is an important issue in today's world influencing quality of life, border-cross trade and commerce. On an international scale, the world of chemical measurements is undergoing major changes. Since a decade initiatives have been taken at an international level and across the measurement sectors to ensure that the measurement science issues are applied in a systematic way. This is done to improve the quality of chemical measurement results and thus make them acceptable everywhere. Only in recent years have the principles of measurement science (metrology) in chemistry received the attention they should. This does not replace the need for many aspects of quality assurance, but compliments this, i.e. bringing a solid foundation to build on.

In the past, emphasis has been nearly exclusively on quality management systems and accreditation. Today, the spotlight is finally back on the basics in measurement science. TrainMiC applies the principles of the International Vocabulary of basic and general terms in Metrology, VIM (ISO, 1993, ISBN 92-67-01075-1) and the Guide to the Expression of Uncertainty in Measurements, GUM (ISO, 1993, ISBN 92-67-10188-9).

3.2 Validation of Measurement Procedures

Validation of a measurement procedure can be regarded as one of the most important parts of the every day laboratory work. In choosing the most promising candidate method, one should consider the expertise in the laboratory, whether it is used routinely and whether the chosen method is fit for the intended purpose. Validation of the measurement procedure increases confidence for users of the measurement procedure and measurement results, and provides information on procedure performance characteristics. According to ISO/IEC 17025 the confirmation of validated procedures is required.

3.3 Traceability of Measurement Results

In this module, various issues concerning traceability of chemical measurement results are addressed. According to VIM, "traceability" means "*properties of the result of a measurement or the value of a standard whereby it can be related to stated references, usually national or international standards, through an unbroken chain of comparisons all having stated uncertainties*". Therefore, every link in the traceability chain should consist of comparisons that are measurements in accordance with the above-proposed meanings, which include the validation of the measurement procedure and the use of reference materials. Not all-chemical measurements are, or should be, traceable to the mole. Other stated references are accepted as well.

3.4 Uncertainty of Measurement Results

Measurement uncertainty is an important ISO/IEC 17025 requirement. This module explains and demystifies the approach of the ISO-GUM (Guide to expression of uncertainty in measurement) to estimate and report the uncertainty of a measurement result obtained following a specific measurement procedure. A clear description of all steps needed for uncertainty evaluation is presented with the respective examples.

3.5 Applied Statistics

The aim of this module is to focus on the few statistical tools that are required for the uncertainty evaluation and the interpretation of inter-laboratory comparisons (ILC). The following topics are presented: average, standard deviation, population distribution (normal, rectangular and triangular), law of uncertainty propagation, type of uncertainties (A and B) and scoring of ILC. The proper understanding of these issues is essential to achieve a correct evaluation of the “combined uncertainty” compliant with GUM. Several examples are discussed in detail.

3.6 Use of Reference Materials

In this module, definition, types of CRMs, their production and use are discussed and critically evaluated, again with a number of examples. The properties of different CRMs: pure substance for calibration, pure substance for matrix matching as well as matrix CRMs are discussed. Several comments on the production procedure and requirement are given as it is assumed that the user of CRMs should be aware of the fact that making CRMs is not a trivial task, but takes skills and proper installations.

The user should know how to look for the most appropriate CRMs and should be aware that producers should provide respective information on traceability, which should be stated and demonstrated. It is concluded that a high quality CRM should have a stated traceability of the certified value, state an ISO-GUM uncertainty of the certified value, both should be demonstrated, and preferably be produced according to a method described under ISO-35.

3.7 Inter-Laboratory Comparisons

The aim of this module is to focus on the different kinds of inter-laboratory comparisons (ILCs) and/or proficiency tests (PTs). The goal is to demonstrate that participating to ILCs or PTs enables to demonstrate ability to measure and should lead to improved quality of results. The results from ILCs or PTs are of crucial interest for laboratories as these provide clear information of its ability to demonstrate reliable results to its customers. It would be pointed out that the participation is either voluntary or forced by external requirements (e.g. legal, accreditation, control bodies). Most ILCs and PT schemes involve comparison of participants results with an assigned value, which has been delivered by a reference laboratory, a sub-group of participants, consensus from the overall population of test results or by some other means. Corrective actions after participation to ILCs are also briefly discussed.

4. Past and next future of TrainMiC

The workshop "*Improving the Scientific Base for Metrology in Chemistry (MIC) in EU Accession Countries*" organised in February 2001 by the IRMM, initiated the TrainMiC concept. Renowned speakers representing established organisations in the field of metrology in chemistry gave plenary presentations. Several working group discussions followed [J.V. Norgaard, I. Papadakis, P. Taylor Accred Qual Assur 6 (2001) 443]. Accession/Candidates Country representatives from the **academia, accreditation bodies and metrology institutes** expressed their needs and expectations in the field of MiC. One of the conclusions was the need to improve the knowledge transfer of the basic MiC concepts - already implemented in the ISO/IEC 17025 - to the laboratory practitioners. The following key words were frequently cited: measurement uncertainty, traceability of a measurement result, validation of measurement procedure and the proper use of certified reference materials. The different ingredients of the TrainMiC curricula were defined.

The first TrainMiC event was held in September 2001 at Sinaia, Romania. Several speakers from different organisations were invited to lecture on the above topics. This interdisciplinary course was appreciated and well perceived by the participants, thus confirming the expectations expressed earlier in Geel. The next task was to prepare a structured and coherent training material to be systematically presented and distributed to participants.

Two brainstorming retreats of several authors in Dendermonde and Mechelen (Belgium) resulted in a set of "TrainMiC" slides that were used throughout the different 2002 courses and constantly refined.

TrainMiC's table of past events

	Date	City	Country	
17	19-20/06/2003	Plovdiv	Bulgaria	
16	11-13/05/2003	Antwerpen	Belgium	for EA technical Assessors
15	24-25/04/2003	Ljubljana	Slovenia	
14	17-18/03/2003	Bucharest	Romania	
13	03-04/03/2003	Ljubljana	Slovenia	
12	26-27/11/2002	Warsaw	Poland	
11	21-22/11/2002	Nicosia	Cyprus	
10	07-08/11/2002	Nicosia	Cyprus	
9	04/09/2002	Blagoevgrad	Bulgaria	
8	20-21/06/2002	Warsaw	Poland	
7	03-05/06/2002	Vilnius	Lithuania	
6	17/12/2001	Sofia	Bulgaria	
5	06/12/2001	Prague	Czech Republic	
4	14-16/11/2001	Ljubljana	Slovenia	
3	05/11/2001	Warsaw	Poland	
2	11-13/10/2001	Maribor	Slovenia	
1	16-19/09/2001	Sinaia	Romania	
	12-13/02/2001	Geel	Belgium	kickoff meeting

The first standardised version of the TrainMiC book was presented at the Warsaw event in November 2002. The “traceability” and “validation” modules were not included, as they required further refinement.

The complete course material was provided to the European Accreditation (EA) technical assessors in May 2003, and to Bulgarian participants in June 2003. The final version of seven modules is presented in the Appendix.

Till August 2003, seventeen TrainMiC events were organised in eight countries, thus reaching 794 participants from many different analytical sectors. The final objective is to arrange two courses per year per country, thus resulting in approximately 20 events per year.

Such an ambitious program requires the recruitment of additional trainers. National trainers were selected to palliate for any language problems during the lectures. When necessary, the modules included in this report will be translated in various languages. The Polish, Bulgarian and Romanian versions are being prepared. TrainMiC courses in local (non-English) languages will be available in 2004.

While TrainMiC is successfully propagating in the new acceding countries, new modules are under development, i.e. one about “sampling” and one on the “interpretation of reported uncertainty”.

TrainMiC events remaining for 2003

	Date	City	Country
21	19-20/11/03	Warsaw	Poland
20	05-06/11/03	Budapest	Hungary
19	09-10/10/03	Warsaw	Poland
18	23-24/09/03	Veliko Tarnovo	Bulgaria

The Training Modules

EUR 20841 EN

- 1 -
General Introduction to Metrology in Chemistry

EUR 20841 EN

TrainMiC
Training in Metrology in Chemistry

Introduction to Metrology in Chemistry

building a metrologicaly sound infrastructure for chemical measurements

TrainMiC
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This course is for people ...

- Performing measurements that
  - Are crossing borders between laboratories
    (e.g. common database of results)
  - Are crossing national borders
    (e.g. trade)
  - Will be used in a legislation context
    (e.g. control lab, enforcement agency)
- Selling *(or considering to sell)* measurement service
- Teaching some of this
- Involved in technical assessments

TrainMiC
Training in Metrology in Chemistry

Overview

- What is Metrology in Chemistry ?
- Why is it needed ?
- What are the differences with Metrology in Physics ?

- Show why it is important
- Define a common language
- Quality of measurement results

The new Global Approach of CIPM-MRA:
focus on metrology & on integration

TrainMiC
Training in Metrology in Chemistry

Metrology = Science of Measurements

Is about understanding the measurement procedure

(<u>not</u> about measuring with <u>smallest</u> achievable uncertainty)

Slide 4

TrainMiC
Training in Metrology in Chemistry

Modern societies use measurements

- in technology
- in trade
- when making regulations
  (*about 40% EU directives involve measurements)*

Metrology is important
and the EC supports it!

Slide 5

TrainMiC
Training in Metrology in Chemistry

Approach in Analytical Chemistry

Traditional / Metrological

Some principles :

- remain the same ...
- some are improved !
- some are changed !

Slide 6

Some ‘traditional’ beliefs

- ☹ My result is correct, but I don’t need to show why
- ☹ it is not necessary to state & demonstrate traceability
- ☹ It is not possible to write model equation
- ☹ It is not possible to use a common approach for uncertainty estimation
- ☹ The smaller the number behind “ ± ” the better my laboratory
- ☹ I did this for long time and I know my business

Slide 7

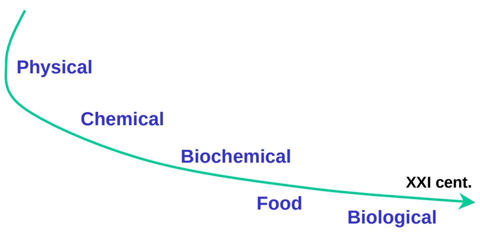
Some common beliefs in metrology

- Limited information: ‘the Truth’ only exists theoretically, as it can only be approximated
- Realism : just do what you can, it will never be perfect
- Transparency: document in an open way, leaving nothing out
- Critical review: there are never problems, unless you look critically
- Standardised/unified language and practices across disciplines & sectors

Slide 8

Metrology in different areas of science

What are you trying to measure?
What is your measurand?



Slide 9

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Metrology, a unified view

Laboratory provides results to Customer/Client

Result = value ± uncertainty Trivial ?

- Uncertainty expresses intrinsic reliability of the result
- ISO-GUM ➔ Common way of estimating uncertainty
- Avoid sector-specific terms *(such as 'intermediate precision', in-between-method precision, etc …)*

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Metrology in Chemistry

Traditional	New
➢ Tracing measurements to some local measurement standard is sufficient	✓ State, establish and demonstrate traceability
➢ Every sector decides on how to express reliability	✓ GUM uncertainty ➔ standardised approach across sectors
➢ Repeating measurements gives all the needed information	✓ Reliability is not improved just by repeating measurements

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Metrology in Chemistry

1. Is related to the fundamentals of analytical chemistry
2. Is needed to obtain good quality measurement results
3. Is the responsibility of every laboratory performing the measurement

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Metrology in Physics v.s. Chemistry

MiP : Often relies on direct-measurements
➔ to a large extent "sample-independent"
(length, mass, temperature, ...)

MiC : various factors affect the quality of results
➔ strongly "sample-dependent"

Difference

Concentration of Cd in..
- ✓ sea water
- ✓ soils
- ✓ blood
- ✓ infant food

TrainMiC
Training in Metrology in Chemistry

Metrology in Physics v.s. Chemistry

MiP : Measurement = comparing a quantity *(e.g. temperature),*
⇨ relate to a unit (e.g. *K*)

Major Impact: (equipment) calibration

Similarity

MiC : Chemical Measurement =
comparing a quantity of analyte *(e.g. [DDT] in milk),*
⇨ relate to a unit (e.g. *mol/kg*; *mg/kg*)

Major impact:
sampling, DDT extraction, calibration solutions,
matrix digestion, and… (equipment) calibration

TrainMiC
Training in Metrology in Chemistry

Basic Glossary

'Measurement' : determining a value of a quantity

'Measurand' : what you try to measure

'Analyte' : the compound, species you measure

'Model' : the equation you use to calculate your final result
(*you always use one!*).
This model is an *(approximating)* description of reality

[VIM, 1993]

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Common language

Quantity	Analyte	Measurand	Unit	Stated Reference
Concentration	DDT	C_{DDT} in soil	ng/L	SI
Amount Content	Pb	w(Pb) in waste water	ng/kg	SI
Count	E.Coli	number of E.Coli/surface	m^{-2}	SI
Activity	Amilase	A(Amilase)	Katal	SI
pH	H^+ ions	$c(H^+)$ in drinking water	pH unit	pH scale
Hardness			Mohs hardness	Mohs scale
Octane index			Octane number	Octane number scale

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A measurement in chemistry involves ...

- ☑ Sample Preparation in the laboratory
  (sampling, digestion, pre-concentration, separation, dilution, …)
- ☑ Calibration
- ☑ (Instrumental) Measurements
- ☑ Critical Data Evaluation
- ☑ Result Reporting: value ± uncertainty

TrainMiC
Training in Metrology in Chemistry

Quality of chemical measurement results today

- A claim is not a demonstrated proof !
- Do not only look at *systems & processes* (e.g. quality management system,written standards), but also at RESULTS

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Training in Metrology in Chemistry

WRONG Conclusions

- …if you use a quality management system in your lab, you *automatically* get better quality results …
- if you use written standards, you *automatically* get better quality results …
- if you use a CRM, you *automatically* get better quality results …

… some 'traditional' simplistic concepts
on the road to better quality chemical measurements !

TrainMiC
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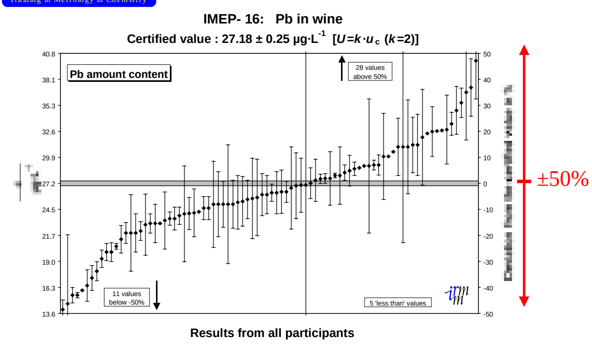
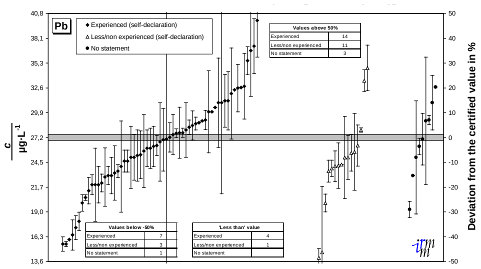
Lead concentration in Wine (IMEP-16)

EC Directive 2001/22
EC Regulation 2676/90
EC Regulation 466/2001
⇨ *threshold value of 0.2 mg Pb /Kg*

TrainMiC
Training in Metrology in Chemistry

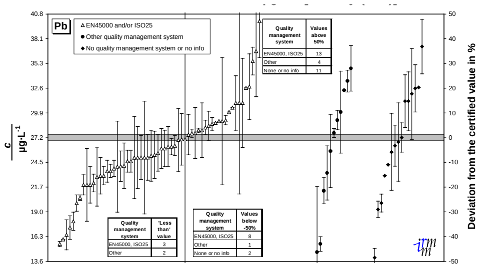


Experienced – Not Experienced



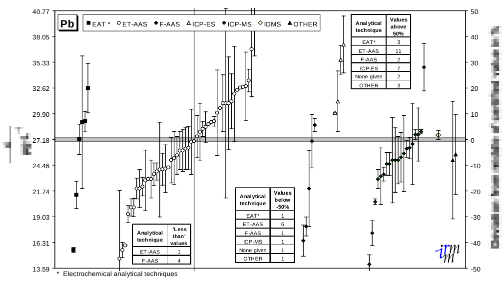
No difference

With – W/O Quality System



No difference

Depends on analytical technique used?



* Electrochemical analytical techniques

No difference

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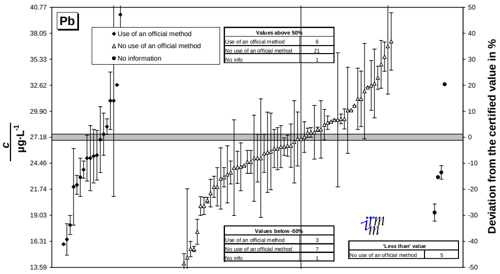
Training in Metrology in Chemistry

With – W/O Official/written standard



No difference

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Training in Metrology in Chemistry

Some better concepts ...

- There are some basic things which apply to any measurement (also chemistry)
- This has a consequence on how measurement scientists 'organise themselves' (preferably NOT on a sector-by-sector level)
- A laboratory also needs to get 'its act together' as an organisation
- Nothing beats experimental proof to substantiate a claim

TrainMiC
Training in Metrology in Chemistry

ISO/EC 17025

Management Requirements

- Staff Training/expertise
- Document control
- Records control
- Instrument reception
- Responsabilities

Technical Requirements

- Validated procedures
- CRMs used
- Uncertainty budget
- Traceability of results
- Inter-Laboratory Comparisons

TrainMiC
Training in Metrology in Chemistry

the Metrology 'Cooking Art'

- ✓ Choose correct measurement system
  take a validated procedure and demonstrate/confirm it
- ✓ Describe measurement system correctly
  (measurement equation)
- ✓ State reference to which results are traceable,
  and demonstrate how
- ✓ Evaluate uncertainty of the results
- ✓ Choose suitable CRMs and use them properly

TrainMiC
Training in Metrology in Chemistry

The new global approach

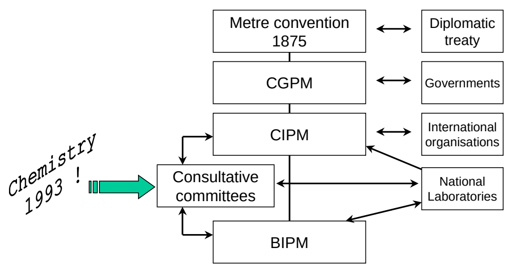
- World wide initiative by metrology organisations
- Under the system of the Metre Convention
- Global approach : set up a general system
  (instead of sector-by-sector !)

Metrology : putting the highlight on
measurement basics/skills again !

TrainMiC
Training in Metrology in Chemistry

The new global approach

Organising measurements on an international scale



The Mutual Recognition Arrangement (MRA)

Industrialised countries set up :

‘once measured,
all measurements
accepted everywhere’

[signed at CIPM, Paris (October 1999)]

Easy to say, difficult to realise

Mutual recognition
of national measurement standards
and of calibration and measurement certificates
issued by national metrology institutes

Paris, 14 October 1999

Comité international des poids et mesures

Bureau international des poids et mesure	Organisation intergouvernementale de la Convention du Mètre

Download from
www.bipm.fr

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http://www.bipm.fr/enus/8_Key_Comparisons/welcome2.html

Mutual Recognition Arrangement (MRA)
JRCB and BIPM key comparison database

At a meeting held in Paris on 14 October 1999, the director of the national metrology institutes (NMIs) of the 33 Member States of the Meter Convention and representatives of two international organisations signed a **Mutual Recognition Arrangement (MRA) for national measurement standards and for calibration and measurement certificates issued by national metrology institutes.**

This Mutual Recognition Arrangement is a response to a growing need for an open, transparent and comprehensive scheme to give users reliable quantitative information on the comparability of national metrology services and to provide the technical basis for a wider agreement negotiated for international trade, commerce and regulatory affairs.

TrainMiC
Training in Metrology in Chemistry

Metrology Organisations

- Your National Measurement Institutes
  (and their partners in chemical measurements)
- Regional Metrology Organisation
  (EUROMET, SIM, APMP …)

☒ Provide ‘ready-made’ products to disseminate traceability (e.g. a value carried by a CRM or by a reference measurement)

☒ Form organised network (e.g. *www.euromet.org*) (can be contacted for information)

☒ Transparency: they need to document and demonstrate measurement capability

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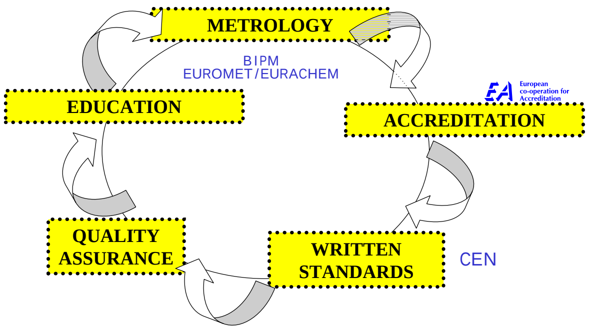
TrainMiC
Training in Metrology in Chemistry

The challenge : INTEGRATION



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1) Questions ?

2) Module Evaluation

Slide 36

- 2 -
Validation of Measurement Procedures

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Validation of measurement procedures

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Content

- What is validation of a measurement procedure ?
- Why procedure validation ?
- Approach to procedure validation ?
- How to perform validation ?
- Outcome?
  - Validation Report,
  - Uncertainty

TrainMiC
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Beware

Difference in terminology between ISO/IEC 17025 and VIM
(Internat. Vocabulary of basic and general terms in Metrology)

- ISO/IEC 17025 uses "method" ➔ *method validation*

- VIM uses "(measurement) procedure" ➔ *procedure validation*

- GLP uses "standard operating procedure", SOP
➔ *SOP validation*

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Validation includes

- ☒ analytical requirements
- ☑ determination of procedure characteristics
- ☒ check that requirements can be fulfilled by the procedure
- ☒ statement on validity

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What is validation ?

Validation is the confirmation by examination and provision of objective evidence that the particular requirements for a specific intended use are fulfilled

(ISO/IEC 17025)

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Validation of measurement procedure

Process of establishing
- performance characterisation
- scope & limitation of a measurement procedure
- identification of the influences

which may change the characteristics and to what extent.

- Which analyte can it determine, in which matrices, in the presence of which interference?
- Within these conditions (to be defined) what uncertainty can be achieved?

The process of verifying that a procedure is fit for purpose
(i.e. for solving a particular analytical problem)

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Intended use

- compliance with regulations
- maintain quality and process control
- make regulatory decisions
- support national and international trade
- support research

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Why do we need it ?

Laboratories should demonstrate they operate within quality system, are technically competent and are able to generate technically valid results

(ISO/IEC 17025)

Three milestones of ISO/IEC 17025:

- ✓ procedure validation
- ✓ traceability of results
- ✓ uncertainty of results

Validation is essential EVEN IF you are not going for accreditation

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Why validation ?

- Provides information on procedure performance characteristics
- Increases confidence:
  - for users of the procedure (analyst)
  - for users of measurement results (customer)

better understanding

validation is a study of the procedure,
NOT of the analyst or of the laboratory performance !

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Often Encountered Terms

- Full Validation:
  where all relevant parameters of the procedure are investigated
- Degree of Validation:
  where only some of the performance parameters are investigated
- Confirmation:
  used in relation to (already validated) standardised procedures. No need for additional validation, just a "confirmation" in your lab.

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Standard & non-standard methods (procedures)

Sources of standard method (procedures):

- procedures published in international, regional, national standards *(ISO, EN, DIN, BS, ASTM, ...)*
- procedures published by reputable organizations in their publications *(AOAC for food and agriculture; ICH for clinical analysis,....)*
- not in scientific literature!

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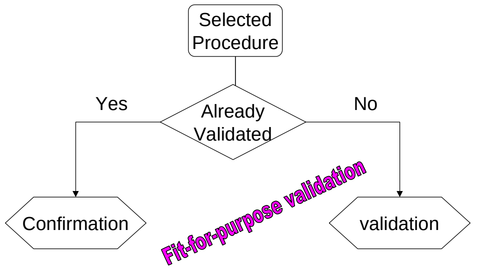
Which procedures should be validated?

- non-standard
- in-house developed
- standard ones used outside their intended scope
- modified standard

Will a validated procedure "automatically" work in my lab?

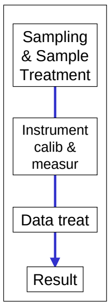
- (First) No, confirmation needed
- (Then) Yes, within the specified conditions

When is a procedure validation needed?



- validate whole procedure
  (from sample preparation to measured signal)
- validate full concentration range
  (intended use!)
- validate all intended types of matrices

Put the effort where it is needed



Required degree of validation

Decide which characteristics are most relevant for your validation (spend effort accordingly!!)

- cholesterol in serum,
  LOD not important (NO),
  uncertainty is important (YES)
  (e.g. better uncertainty of the results ⇨ USA saves 100 M$/year)
- survey of environmental contamination [to find hot spots]:
  range and linearity YES,
  LOD and size of uncertainty NO
- doping control (against limit):
  LOD is critical,
  uncertainty is extremely important;
  range, linearity is not important

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Validation technique...

… recommended by ISO/IEC 17025

- evaluation of uncertainty =
  systematic assessment of the quantities influencing the result
- measurement of CRM
- participation in inter-laboratory comparison
- comparison of results achieved with other procedures

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Use...

- ✓ Standards and/or reference materials
- ✓ Investigate blanks
- ✓ Artificially prepared samples (e.g. spiked)
- ✓ Statistics
- ✓ Common sense

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Checklist

Performance parameters of the procedure

(qualitative): ☐ selectivity, specificity

(*quantitative*):

- ☐ working (linear) range
- ☐ detection & quantification/determination limits
- ☐ sensitivity

Property of the result obtained with this procedure

☐ traceability *(cf. other module)*

☐ uncertainty, considering e.g.
- – recovery
- – robustness
- – repeatability
- – reproducibility

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Selectivity, Specificity

- Selectivity refers to the extent to which the method can be used to determine particular analytes in mixtures or matrices without interferences from other components of similar behaviour

(IUPAC, 2001)

- Specificity is 100% selectivity
- Few, if any methods are specific
- IUPAC recommends that the term specificity should be avoided

(IUPAC, 2001)

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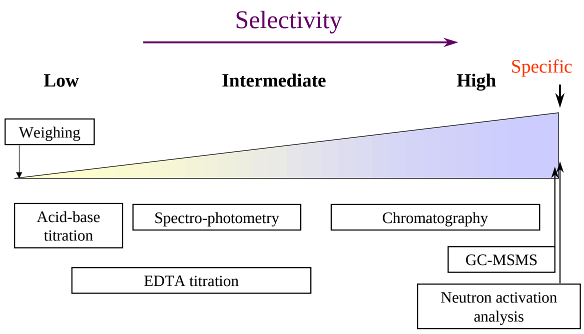
Selectivity, Specificity



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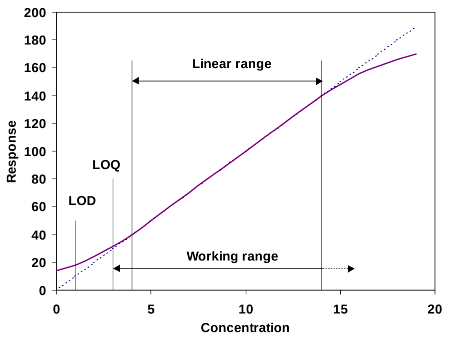
Linearity
Working Range



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Limits of...
Detection (LOD)
Quantification (LOQ)

'Blank'

- instrumental blank
- procedural blank
  (e.g. contamination in digestion, purification)

Calibration equation:

Signal = $b_0 + b_1 * c$

Y_{bl} = Signal of the 'blank' ;

s_{bl}= stdev of the 'blank' in signal domain

$Y_{LOD} = Y_{bl} + 3\, s_{bl}$ ➔ $LOD = (Y_{LOD} - b_0)/b_1$

$Y_{LOQ} = Y_{bl} + 10\, s_{bl}$ ➔ $LOQ = (Y_{LOQ} - b_0)/b_1$

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Reporting of LOD

Detection capability at low concentrations

Analyte…	Analyte… Not present	Analyte… Present
Not detected	True Negative	False Negative ➊
Detected	➋ False Positive	True Positive

➊ Insensitive method? Interference?
➋ Interference? Contamination

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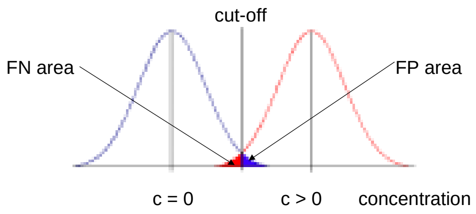
Decisions on LOD

Non-presence of analyte	Presence of analyte



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Sensitivity

- *Definition*:
  The change in the response of a measuring instrument divided by the corresponding change in the stimulus

  (VIM 1993)

- *What it means*:
  The gradient (slope) of the calibration graph

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Recovery (1)

A measure of the trueness of a (measurement) procedure

(IUPAC 1999)

$$R = \frac{observed\_value}{reference\_value}$$

Reference value from:

- CRM $R = \frac{C_{observed}}{C_{CRM}}$
- spike of pure substance $R = \frac{C_{observed} - C_{matrix}}{C_{spike}}$

The closer R is to 1, the smaller the bias in the procedure

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Recovery (2)

The recovery for a particular sample, R, consist of three components combined multiplicatively *(VAM Project 3.2.1)*:

$R = R_m * R_s * R_{rep}$

R_m: mean recovery obtained from the analysis of a CRM or a spiked sample

$u(R_m)$: uncertainty in cert. value / STD of replicate analyses

R_s: correction factor for various matrices

R_{rep}: correction factor for different in behaviour of analyte in spike and real sample with incurred analyte

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Robustness (1)

The robustness (ruggedness) of the measurement procedure is the resistance to change in the result when minor deviations are made from the experimental conditions described in the procedure

Procedure prescribes the limits for experimental parameters

Examples: pH, temperature, concn. of reagent, operator, ...

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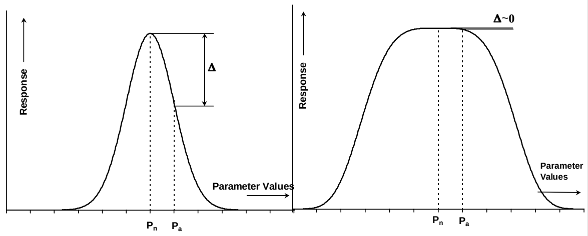
Robustness (2)

Non-Robust Parameter **Robust Parameter**



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Robustness (3)

- Identify variables of method: A,B, C, D etc
- Set-up experiments (Youden/Steiner)
- By systematic changing of one variable, determine effects on result (see table Y/S)
- Review the results to determine optimal conditions
- Procedure improvement from results obtained (gives also information on influence quantities)

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Robustness (4)

Experiment no.:		1	2	3	4	5	6	7	8
Parameters									
A	pH	5	5	5	5	7	7	7	7
B	temp.	25	25	35	35	25	25	35	35
C	reaction time	30	60	30	60	30	60	30	60
D	reagent 1	1	1	2	2	2	2	1	1
E	reagent 2	1	2	1	2	2	1	2	1
F	age of column	old	new	new	old	old	new	new	old
G	personnel	xx	yy	yy	xx	yy	xx	xx	yy
	Response	r	t	u	v	w	x	y	z

ANOVA: *A, B, and D are non-robust*

- provide basic/preliminary information
- evaluate whether the model equation is valid
- better instructions for operators

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LOGO

Validation Report

- Procedure: Cadmium determination by GF-AAS
- Measurand: Cadmium concentration in food products
- Source of the Method: Developed in-house
- Intended Use: Screening of food samples
- Matrix: food and feed products
- Analytical protocol: Microwave digestion, followed by GF-AAS
- Calibration: with solution standards from Supplier-ZZZ
- Working Range: up to 20 ng/g
- LOD: 1 ng/g
- LOQ: 3.5 ng/g
- Selectivity: Free from interference up to 1000 ng/g of Chloride
- Traceability: to SI. Established by calibration Demonstrated by measurement of certified reference material-YYY
- Typical Uncertainty: 10%, see Uncertainty budget (Annex)

Name		
Function	*Laboratory Assistant*	*Head of Laboratory*
Signature		
Date		

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Can I do the work?

Case	Request	Answer
1	Cd in Milk expected: 0.5 to 1.5 ng/g	NO ➔LOD
2	Cd in sea water expected: 5 to 10 ng/g	NO ➔ acceptable working range BUT ➔ high Cl content
3	Cd concentration in lake waters expected 5 - 10 ng/g	YES ➔fit for purpose

- 3 -
Traceability of Measurement Results

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Traceability of Measurement results

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Scope of the lecture

- What is Traceability?
- What is it needed for?
- How to establish Traceability?
- How to demonstrate Traceability?

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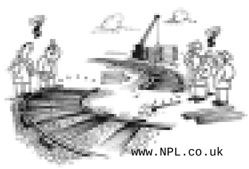

Validation *(method fit-for-purpose)*

Quality of measurement result

Traceability
(my result is comparable - common reference)

Uncertainty Budget
(How well I know the result)

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Traceability of ...

Not concerned by:

- ☒ … sample in the lab
- ☒ … documents in a filing system

Not applicable to:

- ☒ … institution
- ☒ … method

Relevant for

- ☑ … measurement results
- ☑ … reference values

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Definition

Traceability is a property of the result of a measurement or the value of a standard whereby it can be related to stated references, usually national or international standards, through an unbroken chain of comparisons all having stated uncertainties.

[VIM, 6.10]

❶ of the result
❷ related to stated references
❸ unbroken chain of comparisons
❹ stated uncertainties

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Stated reference

Meaningful comparisons between measurements are only possible if the results are expressed in the same units (measurement scale)

- SI units *(m, kg, s, A, K, mol, cd) or combination*
- to best internationally agreed reference (if no SI), such as:
  - ✓delta scale for isotopic measurements
  - ✓ pH scale
  - ✓ the scale of octane numbers for petroleum fuel
  - ✓ spectrophotometric measurement of lightness of coatings (CIELab system, Lovibond,…)

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Do we really need traceability?

Traceability to the same
stated reference
is of essential importance for
comparability of the results.

Comparability (able to compare) and reliability (trustworthiness) of measurement results between different laboratories are of outmost importance if they are to form an acceptable basis for decision making and the implementation of regulations.

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Stating ... is a claim
&
Establishing ... is what I do in my lab
&
Demonstrating ... and I can show it

... Traceability

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Establishing traceability

① Specifying the measurand

② Choosing a suitable
- measurement procedure
- model equation

③ Demonstrating (validation) that:
- the model equation is adequate (all significant influence quantities have been taken into account)
- the measurement conditions are adequate

④ Establishing traceability for each influence quantity:
- Choosing appropriate reference standards
- Calibrating using the standards

⑤ Evaluating uncertainty

[EURACHEM/CITAC Guide, 2002]

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Reminder

Analyte: Article that is the subject of a measurement *(GLP)*
e.g. cholesterol

Measurand: Particular quantity subject to measurement (VIM,2.6)
e.g. concentration of cholesterol in serum

- Validation and Traceability are "correlated"
  validation is part of establishing traceability
- Traceability and Uncertainty are "correlated"
  "unbroken" chain of comparison &
  "unbroken" uncertainty propagation

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Common language

Quantity	Analyte	Measurand	Unit	Stated reference
concentration c	DDT	*c*(DDT) in soil	ng/kg	SI
content *w*	Pb	*w*(Pb) in waste water	ng/L	SI
count	E. Coli	Number of E.Coli per unit surface	m^{-2}	SI
activity	amylase	*A*(amylase)	Katal	SI
pH	H^+ ions	$c(H^+)$ in waste water	pH number	pH scale

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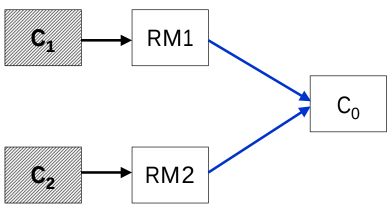
Associativity of Comparability – choosing reference standard ④



Are C_1 & C_2 Comparable?

Yes, through common reference

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Traceability

- to be established for each input quantity specified in the procedure / model equation
- established by calibration using appropriate standards

Calibration:
Set of operations which establish, under specified conditions, the relationship between values indicated by a measuring instrument - (including chemical steps) and the corresponding known values of the measurand.

Must be performed by reference standards with demonstrated traceability and adequately small uncertainty.

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Calibration Hierarchy

Metrological Traceability ↑ Tools	Service Providers — Uncertainty ↓
• Primary Std • International Std • National Std • Reference Std • Transfer Std • Travelling Std • Working Std	• BIPM • Nat. Metrology Institutes • Accredited Calib. Labs • Company (in-house) - calibration centre - test laboratory

[ILAC-G2:1994]
Traceability of Measurements

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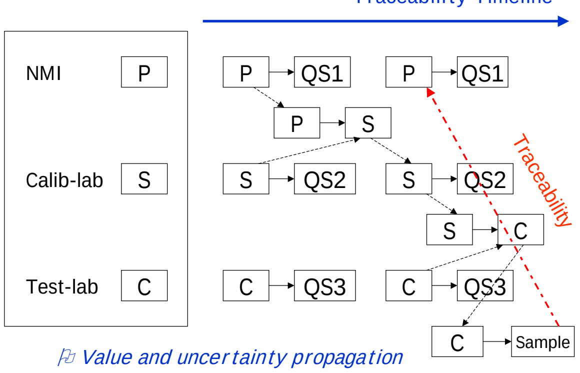
C.D.EHRLICH, S.D.RASBERRY J.Res. NIST 103 (1998) 93

Traceability Timeline



Value and uncertainty propagation

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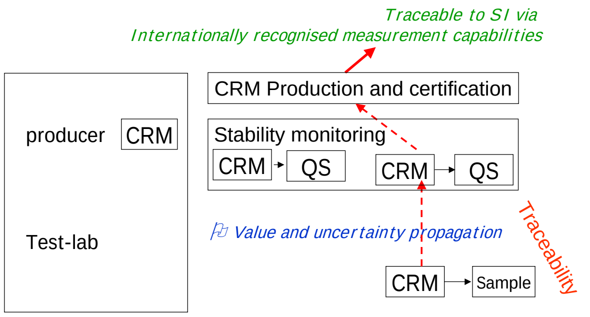
Idem for Certified RM

Traceability Timeline



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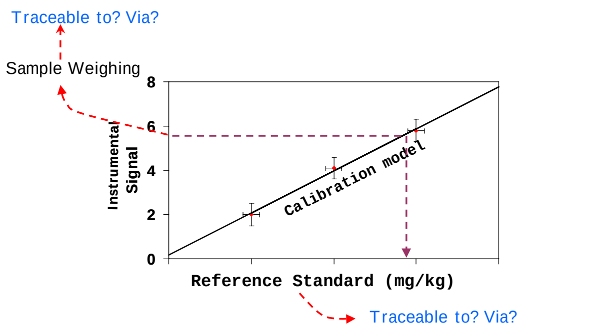
Result Traceable to Value of Reference Standard



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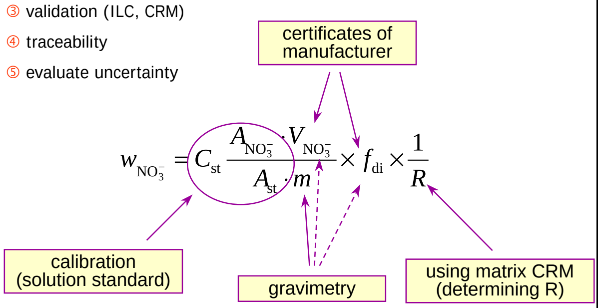
Demonstrating Traceability

① measurand: content of nitrate in plants
② suitable model equation
③ validation (ILC, CRM)
④ traceability
⑤ evaluate uncertainty



$$w_{NO_3^-} = C_{st}\frac{A_{NO_3^-}\cdot V_{NO_3^-}}{A_{st}\cdot m}\times f_{di}\times\frac{1}{R}$$

- 4 -
Uncertainty of Measurement Results

EUR 20841 EN

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Uncertainty of Measurement Results

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Overview

- **Definitions**
- **Uncertainty - what for?**
- **Limitation of measurements**
- **GUM procedure for uncertainty evaluation**
- **Examples**

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When should you evaluate uncertainties of measurement results ?

- When a procedure is introduced inside your laboratory
- When a critical factor changes in the procedure (instrument, operator, …)
- During / together with procedure validation

➔ An individual evaluation process is NOT needed for every individual result produced !

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ISO Definition of Uncertainty

‘a parameter associated with the result of a measurement, that characterises the dispersion of the values that could reasonably be attributed to the *measurand* ’

Result = Value ± uncertainty

(22.7 ± 4.8) mg/kg

The value is between 17.9 and 27.5 mg/kg
(cf. *range, interval*)

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Why do we need uncertainty?

- It is required by ISO 17025 - Accreditation
- The uncertainty of the result demonstrates the metrological QUALITY of the measurements *(not measuring with the smallest achievable uncertainty)*
- It improves the knowledge about the measurement procedure
- In laboratory → document in transparent way the measurement procedure
- For end-user → give the result with proper confidence
- To allow comparison of results

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Why do we need uncertainty ? (2)

- A well documented uncertainty statement underpins your results and provides transparency!
- Identify major uncertainty contributors - find out ways to improve the procedure
- Demonstrate compliance with limits (legal or contractual) and the establishment of acceptance criteria

⇨ Your best defence in discussions!

☒ Repeating the measurement 2, 10 or 100 times does not give you all information to have reliable results!

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~~True Value~~ or best estimate of True Value

- We can approach to measure the true value by measuring the "the best estimate"

  ➔ aiming to know true value

  - *i.e.* alcohol content of blood
  - *i.e.* nitrate content of drinking water
  - *i.e.* acrylamide content of crisp bread
  - *i.e.* lead content of wine

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Are results different?

No results without uncertainty !

```
R1 = 10.6 mg/kg
R2 = 11.6 mg/kg
```

• Traditional approach: precision

```
R1 = (10.6 ± 0.2) mg/kg
R2 = (11.6 ± 0.3) mg/kg
```

• GUM approach: uncertainty propagation (combined unc.) to take into account the contribution of all components

```
R1 = (10.6 ± 0.7) mg/kg
R2 = (11.6 ± 0.7) mg/kg
```

No statistical tests required by GUM *(almost)* …/…
cf. Visual comparison ➔ overlapping ranges Y/N ?

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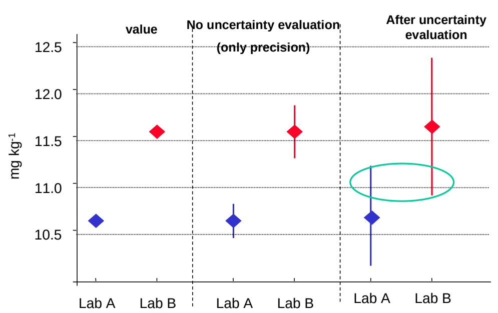
Are these results different?



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GUM does not require
statistical tests
unless you need it …

“If it is deemed useful for the intended users of the measurement result, ……, one may indicate - the estimated effective degree of freedom…” – *[GUM 7.2.1]*

- ☑ when comparing results
- ☑ for legal requirements
- ☑ requested by customer

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repeatability < reproducibility < combined uncertainty

Don’t forget

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What is new in GUM ?

- GUM is guide for a transparent, simple and standardised documentation of the measurement procedure
- Using uncertainty evaluations, such as *type A (measured in the lab)* and *type B (other)*

Do NOT use random & systematic errors !

- The use of Combined/expanded Uncertainty

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Uncertainty "Type"

Type A evaluation of uncertainty:

statistical analysis of series of observations.

Type A standard uncertainty is measured from repeatability experiments and is quantified in terms of *the standard deviation* of the measured values

Type B evaluation of uncertainty:

by *other means* than statistical analysis

(previous experiments, literature data, manufacturer's information)

[GUM, 1993]

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Understanding the measurement !

"…The evaluation of uncertainty is neither a routine task nor a purely mathematical one; it depends on detailed knowledge of the nature of the measurand and of measurement…"

[GUM § 3.4.8]

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How to apply GUM uncertainty ?

Document the data you used as input for measurement!!

"…The pool of information may include:

- ✓ previous measurement data;
- ✓ validation data
- ✓ experience with or general knowledge of the behaviour and properties of relevant materials and instruments;
- ✓ manufacturer's specifications
- ✓ data provided in calibration and other certificates;
- ✓ uncertainty assigned to reference data taken from handbooks"

[GUM § 4.3.1]

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What do you need to know ?

some basic statistics

- average of the set of data;
- standard deviation;
- law of propagation;
- distribution (normal, rectangular, triangular…)

(cf. statistics module)

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The 10-steps GUM Sequence

1 - Define the Measurand

2 - Describe the Model Equation *(for the measurement procedure)*

3 - Identify (all possible) sources of uncertainty

4 - Evaluate all input quantities

5 - Evaluate the standard uncertainty (1s) of each input quantities

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The 10-steps GUM Sequence
(continued)

6 - Calculate the value of the measurand (using the equation model)

7 - Calculate the combined standard uncertainty of the result

8 - Calculate the expanded uncertainty (with a selected *k*)

9 - Analyse the uncertainty contribution index *(THINK !!)*

10- Document all steps in a Report.

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Experimental Protocol

Determination of Nitrate by Ion Chromatography in Plant material

Sample treatment
- Sample weighing, *m*
- Extraction, *R*
- Preparing the sample solution, V_{NO3-}
- Dilution of the sample solution, f_{di}

↓

Instrumental measurement, A_{NO3-}

Preparing the standard solution, C_{st}

↓

Instrumental measurement, A_{st}

↓

Calculation of the result, Q_{NO3-}

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Step 1 - Definition of "Measurand"

Measurand = particular quantity subject to measurement

[VIM 2.6 / GUM B.2.9]

Example: content of NO_3^- in (mg/g)

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Step 2 - Model Equation

The model of the measurement procedure is a functional relation between input quantities and output quantity (result)

$$Y = f(X_1, X_2, ..., X_n)$$

Measurement MODEL is the equation you use for the calculation of your result !

You have it already

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What are input quantities?

The output quantity Y depends on input quantities $X_1, X_2, \ldots, X_n$:

$$Y = f(X_1, X_2, \ldots, X_n) \quad [GUM\ 4.1.2]$$

Input quantities (X_i) may be quantities whose value and uncertainty are directly determined in the current measurement (Type A, *statistical analysis of series of observation*) or brought into the measurement from external sources (Type B, *previous experiments, literature data, information from manufacturer*)

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Model Equation

$$Q_{NO_3^-} = C_{st} \frac{A_{NO_3^-} \cdot V_{NO_3^-}}{A_{st} \cdot m} \times f_{di} \times \frac{1}{R}$$

Q_{NO3-}	*nitrate content of the sample (mg/g)*
C_{st}	*nitrate concentration in standard solution (mg/l)*
A_{NO3-}	*peak area for sample solution*
A_{st}	*peak area for standard solution*
V_{NO3-}	*volume of sample solution (l)*
m	*mass of the sample (g)*
f_{di}	*dilution factor (no units);*
R	*recovery factor (cf. sample preparation)*

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Step 3 - Possible Sources of Uncertainty

- ☑ recovery of analyte from a complex matrix
- ☑ storage conditions
- ☑ reagent purity
- ☑ assumed stoichiometry
- ☑ sampling
- ☑ measurement conditions
- ☑ instrument response
- ☑ bias of instrument
- ☑ instrument resolution
- ☑ uncertainty of standards and CRM's
- ☑ variations in repeated observations

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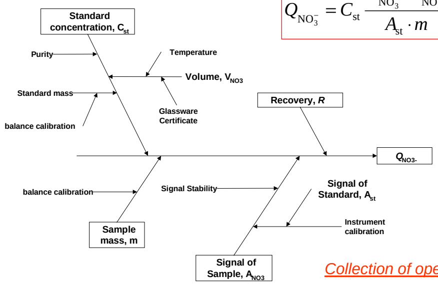
Step 3 - Possible Sources of Uncertainty

$$Q_{NO_3^-} = C_{st}\frac{A_{NO_3^-}\cdot V_{NO_3^-}}{A_{st}\cdot m}\times f_{di}\times\frac{1}{R}$$



Collection of operations

Slide 25

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Step 4 - Input Quantities Uncertainty (evaluation type A & B)

- repeated observation (A)
- validation experiments (A and/or B)
- manufacturers' specifications (B)
- calibration certificates (B)
- results of interlaboratory method validations (B)
- from experience and/or literature (B)

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Step 5 - Convert to Standard Uncertainties

Before combining, all uncertainty contributions must be expressed/converted as "estimated" standard uncertainty

when available as:

- standard deviation: use as is
- confidence intervals: convert
- stated range: convert
- expanded uncertainties: convert

See Module "Statistics"

Slide 27

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Step 6 - Calculate Value of Measurand

Use model equation to calculate the value of output quantity Y (Q_{NO3-})

$$Q_{NO_3^-} = C_{st} \frac{A_{NO_3^-} \cdot V_{NO_3^-}}{A_{st} \cdot m} \times f_{di} \times \frac{1}{R}$$

Example

$$Q_{NO_3^-} = 0.801 \times \frac{0.0131 \times 0.1000}{0.0232 \times 1.142} \times 10 \times \frac{1}{0.78}$$

$$\boxed{Q_{NO_3^-} = 0.508 \quad mg/g}$$

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Step 7 - Combined Standard Uncertainty

When there is no correlation between input quantities the combined standard uncertainty is evaluated as the square root of the combined variance according to:

$$u_c^2(Y) = \sum \left(\frac{\partial f}{\partial X_i}\right)^2 \cdot (u(X_i))^2$$

Law of Uncertainty propagation

where
$u_c(Y)$ = combined standard uncertainty
$u(X_i)$ = standard uncertainty of each input quantity

Can be done by spreadsheet or by dedicated software!

See Module "Statistics"

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Combined Standard Uncertainty

$$u_{c,r}(Q_{NO_3^-}) = \sqrt{\begin{aligned} & RSu(C_{st})^2 + RSu(A_{NO_3^-})^2 + RSu(A_{st})^2 + \\ & + RSu(V_{NO_3^-})^2 + RSu(m)^2 + RSu(f_{di})^2 + RSu(R)^2 \end{aligned}}$$

where $RSu(X_i) = u(X_i)/X_i$ *(relative standard uncertainty)*

$$u_{c,r}(Q_{NO_3^-}) = \sqrt{\begin{aligned} & \left(\frac{0.00058}{0.801}\right)^2 + \left(\frac{0.0003}{0.0131}\right)^2 + \left(\frac{0.0006}{0.0232}\right)^2 + \\ & + \left(\frac{0.0003}{0.1000}\right)^2 + \left(\frac{0.00058}{1.1420}\right)^2 + \left(\frac{0.023}{10.000}\right)^2 + \left(\frac{0.04}{0.78}\right)^2 \end{aligned}}$$

$u_c(Q_{NO3-}) = u_{c,r}(Q_{NO3-}) \times Q_{NO3-} = 0.032$ mg/g

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Step 8 - Expanded Uncertainty

The expanded uncertainty, U, is obtained by multiplying the combined standard uncertainty $u_c(y)$ by a coverage factor k:

$$U = k * u_c$$

The result is then expressed as: $\boxed{\text{Result} = y \pm U \ (k = ??)}$

For the example: $Q_{NO3-} = (0.51 \pm 0.06)$ mg/g , $k = 2$

- the best estimate of the value attributed to the measurand is "y",
- the interval $[y - U , y + U]$ is the range that may be expected to encompass a large fraction of the distribution of values that could reasonably be attributed to the measurand.

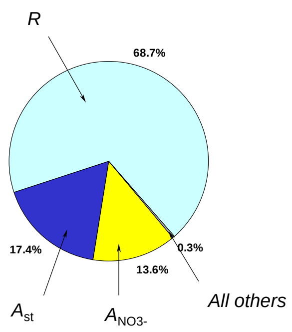
Step 8 - Expanded Uncertainty (2)

- Expanded uncertainty gives a more realistic range of possible values.
- The coverage factor usually used is $k = 2$, representing a coverage of about 95%, if the distribution is normal

Standard uncertainty should be used inside the laboratory
(to apply uncertainty propagation)

Expanded uncertainty is more realistic range given for the end-users of the results

Step 9 - Uncertainty Contributions



Major Contributor :

- Type B? ☹
- Type A? ☺
- Replicates?
- Much work?
- Control Charts?

Think!

See Module "Statistics"

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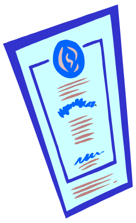
Step 10 - Reporting Results



Q_{NO3-} = (0.51 ± 0.06) mg/g (*)

(*)
the reported uncertainty is an expanded uncertainty calculated using a coverage factor of k = 2, which gives a level of confidence of approximately 95%

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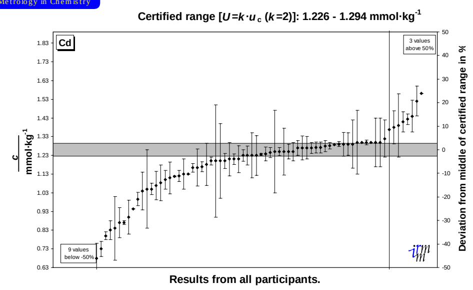

Metrologists obsessed by small uncertainties ?

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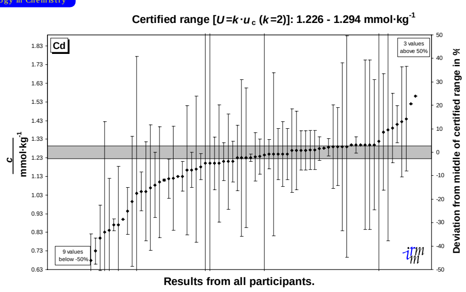

Learning how to apply GUM:
Better sell your results with
reliable uncertainty statement !

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Summary: about uncertainty

- Uncertainty of measurement results evaluation according to the GUM is a useful and accepted concept to evaluate results of a measurement;
- It allows others (e.g. assessors) to understand what & how things were done
- It allows the analyst to combine prior knowledge and observations in a consistent and well defined way;
- It doesn't requires to measure with smallest achievable uncertainty, but with the most realistic one

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Uncertainty adopted and accepted by ...

- This concept is adopted and accepted by international institutions, such as NMIs and BIPM
- Is required under ISO 17025 for accreditation
- IUPAC, OIML and accreditation community such as EA and ILAC have accepted this concept
- CEN is incorporating these concepts

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1) Questions ?

2) Module Evaluation

- 5 -

Applied Statistics

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Applied Statistics

Slide 1

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Statistics, why and when?

- Evaluation of uncertainty of results according to ISO-GUM
- Evaluation of Inter-Laboratory Comparison (ILC)
- Quality assurance:
  - method performance (accuracy; precision; ...)
- Optimisation of measurement procedures

Slide 2

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Statistics for evaluation of uncertainty

Slide 3

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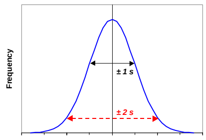
Normal distribution



For a set of n values x_i

Mean Value (average) $\bar{x} = \frac{1}{n}\sum_{i=1}^{n}(x_i)$

Standard Deviation $s(x_i) = \sqrt{\frac{1}{n-1}\cdot\sum_{i=1}^{n}(x_i - \bar{x})^2}$

Variance of the mean $V(x_i) = s^2(x_i)$

Relative Standard Deviation $RSD = \frac{s(x_i)}{\bar{x}} \quad (absolute \quad or \ \%)$

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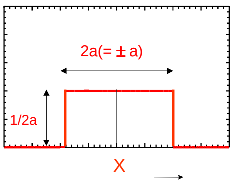
Rectangular distribution

The Value is between the limits

$a_{-} \ldots a_{+}$

The expectation

$y = x \pm a$



Assumed standard deviation:

$s = a / \sqrt{3}$

One can only assume that it is equally probable for the value to lie anywhere within the interval

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Example of Rectangular distribution

"*It is likely that the value is somewhere in that range*"

Rectangular distribution is usually described in terms of:
the average value and the range (±a)

Certificates or other specification give limits where the value could be, without specifying a level of confidence (or degree of freedom).

Examples:
Concentration of calibration standard is quoted as (1000 ± 2) mg/l
Assuming rectangular distribution the standard uncertainty is:

$$s = u(x) = a / \sqrt{3} = 2 / \sqrt{3} = 1.16 \ \ mg / l$$

The purity of the cadmium is given on the certificate as (99.99 ± 0.01) %
Assuming rectangular distribution the standard uncertainty is:

$$s = u(x) = a / \sqrt{3} = 0.01 / \sqrt{3} = 0.0058 \ \%$$

Slide 6

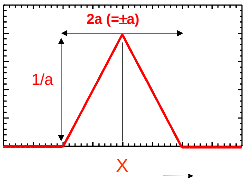
Triangular distribution

Distribution used when it is suggested that values near the centre of range are more likely than near to the extremes

$$y = x \pm a$$

Assumed standard deviation:

$$s = a \cdot 1 / \sqrt{6}$$



Slide 7

Example of Triangular distribution

Values close to x are more likely than near the boundaries

The available information concerning the value is less limited than for rectangular distribution.

Example *(volumetric glassware)*

The manufacture quotes a volume for the flask of (100 ± 0.1) ml at T = 20° C.
Nominal value most probable!
Assuming triangular distribution the standard uncertainty is:

$$s = u(x) = a \cdot 1/\sqrt{6} = 0.1/\sqrt{6} = 0.04\ ml$$

In case of doubt, use the rectangular distribution

Slide 8

Confidence Interval

The individual observations are distributed about the best estimate of the “True Value” with a spread, which depends on the precision

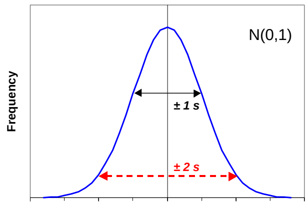
The estimate of the “True Value” (μ) lies within the confidence interval *(CI)*, with a probability of *(1-α)*, *having “n-1”* degrees of freedom:
(where n = number of replicates)

$$\mu = \bar{x} \pm (1 - \alpha)\ \%\ CI\ (n)$$

$$95\ \%\ CI = t(0.05, n - 1) * s / \sqrt{n}$$

Slide 9

Confidence Interval (2)



$\mu \pm 1s$	68 %
$\mu \pm 2s$	95 %
$\mu \pm 3s$	99.7%

Law of "Uncertainty Propagation" *without correlation*

$Y = f(X_1, X_2, \ldots\ldots, X_n)$

$$u_c^{\,2}(Y) = \sum \left(\frac{\partial f}{\partial X_i}\right)^2 \cdot \left(u(X_i)\right)^2$$

$C = (a + b)$

$C = (a - b)$

$$\Rightarrow \quad u(C) = \sqrt{u(a)^2 + u(b)^2}$$

$C = (a * b)$

$C = (a / b)$

$$\Rightarrow \quad \frac{u(C)}{C} = \sqrt{\left(\frac{u(a)}{a}\right)^2 + \left(\frac{u(b)}{b}\right)^2}$$

Different estimation of uncertainty

Type A evaluation of uncertainty:

statistical analysis of series of observations.

Type A standard uncertainty is measured from repeatability experiments and is quantified in terms of *the standard deviation* of the measured values

Type B evaluation of uncertainty:

by *other means* than statistical analysis

(previous experiments, literature data, manufacturer's information)

[GUM, 1993]

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According to GUM...

When there is no correlation between input quantities the combined standard uncertainty is evaluated as the square root of the combined variance according to the law of uncertainty propagation:

$$u_c^2(y) = \sum \left(\frac{\delta f}{\delta x_i}\right)^2 \cdot (u(x_i))^2$$

Expanded Uncertainty, U, is obtained by multiplying the combined standard uncertainty by a coverage factor k:

$$U(y) = k * u_c(y)$$

often $k = 2$

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An uncertainty is given in the form of Standard Deviation *[s = u(x)]*

$$R = \overline{x} \pm \Delta x$$

But what is Δx ?

- Standard deviation ?
- Rectangular distribution uncertainty ?
- Triangular distribution uncertainty ?
- Confidence interval w/o specified degree of freedom ?
- Confidence Interval with specified degree of freedom ?
- Combined Uncertainty *?*
- Expanded uncertainty *? Is "k" specified ?*

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Standard deviation
of a single measurement

0. Experimental Measurement ➔ uncertainty (Type A) !

1. Single measurement with several instrumental replicates:

$$R = \overline{x} \pm s$$

s
- provided by the instrument
- calculated from (instrumental) replicates

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Standard deviation of n independent measurements

2. Several (**n**) independent measurements
with several instrumental replicates

$$R_i = \bar{x}_i \pm s_i$$

assuming that ALL s_i are similar *(= s)*

$$R_i = \bar{x}_i \pm s$$

$$R = (\bar{R}_i) \pm s_{mean} = (\bar{R}_i) \pm \frac{s}{\sqrt{n}}$$

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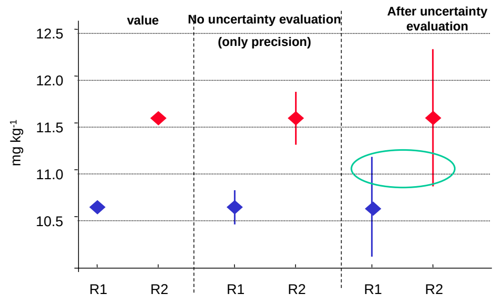
Are these results different?



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(Traditional) Statistical Approach

Measurement Cd content in plant
3 digested samples

1st Digestion : 20.5 mg/kg 2nd Digestion : 21.0 mg/kg 3rd Digestion : 21.5 mg/kg	mean [Cd] = 21.0 mg/kg (stdev) s = 0.5 mg/kg

(mean ± stdev) C_{Cd} = (21.0 ± 0.5) mg/kg
(mean ± 95% CI) C_{Cd} = (21.0 ± 1.2) mg/kg, with n = 3

t(0.05,2)= 4.3

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GUM Approach

Measurement Cd content in plant
3 digested samples

1st Digestion : 20.5 mg/kg
2nd Digestion : 21.0 mg/kg
3rd Digestion : 21.5 mg/kg

⇒ mean [Cd] = 21.0 mg/kg
Combined unc. u_c = 2.1 mg/kg

Uncertainty Budget calculation ➔ Combined Uncertainty
(including contribution from all parameters)

mean ± Expanded uncertainty
C_{Cd} = (21.0 ± 4.2) mg/kg, with k = 2

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Statistics for method performance studies

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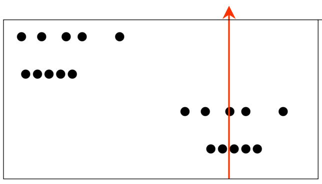
Best estimate of the "True Value"



Accurate?	Precise?
no	no
no	yes
yes	no
yes	yes
(close)	*(scatter)*

Precision: The closeness of agreement between independent test results obtained under stipulated conditions [ISO 5725]

Precision ↗ ⇒ Scatter ↘ ⇒ uncertainty ↘

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Accuracy

Closeness of agreement between a test result of a measurement and the accepted reference value (ISO 3534-1)

Accuracy is not given by the spread of a normal distribution, but by the deviation of the arithmetic mean of a series of results from accepted reference value

Accuracy ↗ ⇒ Deviation ↘ (zero)

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Repeatability

Precision recorded under repeatability conditions:

- same laboratory, analyst, equipment, time (short interval)

Typically used for studying variation

within a batch or between replicated measurements.

Within-run precision = Repeatability

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Reproducibility

Precision recorded under reproducibility conditions:

- different laboratory, analyst, equipment, time (short interval)

Typically used for studying variation

on measurements made between laboratories.

Between-run precision = Reproducibility

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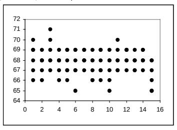
Anova Single factor

Replicates		1	2	3	4	5	6
Vials	1	66	68	67	69	70	69
	2	66	67	68	68	68	69
	3	71	67	68	69	68	70
	4	66	68	67	68	68	69
	5	67	67	66	69	69	68
	6	65	67	67	69	68	69
	7	67	68	68	68	69	69
	8	67	66	66	68	68	69
	9	67	67	66	69	68	69
	10	66	65	67	68	69	68
	11	67	67	69	68	68	70
	12	67	68	69	69	68	69
	13	67	67	68	69	68	68
	14	67	68	68	69	68	69
	15	65	66	65	68	68	67



$R = 2^* \sqrt{2} * s_R$

$r = 2^* \sqrt{2} * s_r$

SUMMARY

Groups	Count	Sum	Average	Variance
1	6	409	68.2	2.2
2	6	406	67.7	1.1
3	6	413	68.8	2.2
4	6	406	67.7	1.1
5	6	406	67.7	1.5
6	6	405	67.5	2.3
7	6	409	68.2	0.6
8	6	404	67.3	1.5
9	6	406	67.7	1.5
10	6	403	67.2	2.2
11	6	409	68.2	1.4
12	6	410	68.3	0.7
13	6	407	67.8	0.6
14	6	409	68.2	0.6
15	6	399	66.5	1.9

ANOVA

Source of Variation	SS	df	MS	F	P-value	F crit
Between Groups	26.2	14	1.87	1.34	0.207	1.83
Within Groups	104.8	75	1.40			
Total	131.0	89				

repeatability stdev	s_r	1.18	=sqrt(MSW)
reproducibility stdev	s_R	1.21	=sqrt(MSW+(MSB-MSW)/N)
			(n replicates)

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Statistics for Inter-Laboratory Comparison (ILC), Proficiency Testing (PT)

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(Traditional) Z-score

$$Z = \frac{x_{lab} - x_{ref}}{"\ s\ "}$$

Difference ➔ distance ➔ accuracy

"Normalized" versus ...

- Target performance *(i.e. 5%)*
- Reference uncertainty (nominal value)
- Inter-Laboratory Comparison reproducibility

Performance evaluation:

```
0 <|Z|< 2 : good
2 <|Z|< 3 : warning ➔ preventive action
    |Z|> 3 : unsatisfactory ➔ corrective action
```

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En-score according to GUM

$$En = \frac{x_{lab} - x_{ref}}{\sqrt{(u_{lab}^2 + u_{ref}^2)}}$$

“Normalized” versus ...

propagated combined uncertainties

Performance evaluation:

```
0 <|En|< 2 : good
2 <|En|< 3 : warning ➔ preventive action
   |En|> 3 : unsatisfactory ➔ corrective action
```


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The Uncertainty Budget
Step-by-step Tutorial

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❶ Model: $Y = X_1 * X_2 / (X_3 * X_4)$ *part 1*

❷

RSD	stdev	value	description
??	0,02	2,46	**X1**
3,0%	??	4,32	**X2**
??	0,11	6,38	**X3**
2,3%	??	2,99	**X4**

❸

RSD	stdev	value	description
0,8%	0,02	2,46	**X1**
3,0%	0,13	4,32	**X2**
1,7%	0,11	6,38	**X3**
2,3%	0,07	2,99	**X4**

❹

RSD	stdev	value	description
0,8%	0,02	2,46	**X1**
3,0%	0,13	4,32	**X2**
1,7%	0,11	6,38	**X3**
2,3%	0,07	2,99	**X4**
??	**??**	**0,557**	Result

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❶ Model: $Y = X_1 * X_2 / (X_3 * X_4)$ *part 2*

❺

RSD	stdev	value	description	X1	X2	X3	X4
0,8%	0,02	2,46	**X1**		2,46	2,46	2,46
3,0%	0,13	4,32	**X2**	4,32		4,32	4,32
1,7%	0,11	6,38	**X3**	6,38	6,38		6,38
2,3%	0,07	2,99	**X4**	2,99	2,99	2,99	
??	**??**	**0,557**	Result				

❻

RSD	stdev	value	description	X1	X2	X3	X4
0,8%	0,02	2,46	**X1**	2,48	2,46	2,46	2,46
3,0%	0,13	4,32	**X2**	4,32	4,45	4,32	4,32
1,7%	0,11	6,38	**X3**	6,38	6,38	6,49	6,38
2,3%	0,07	2,99	**X4**	2,99	2,99	2,99	3,06
4,2%	**0,024**	**0,557**	Result	0,562	0,574	0,548	0,544

x+Δx

❼

diff	0,005	0,017	-0,009	-0,013	0,001

$$u_c = \sqrt{\sum_i (y_i - y)^2}$$

sumsq($diff_i$)

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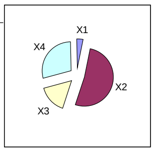
❶ Model: $Y = X_1 * X_2 / (X_3 * X_4)$ *part 3*

RSD	stdev	value	description	X1	X2	X3	X4	
0,8%	0,02	2,46	**X1**	2,48	2,46	2,46	2,46	
3,0%	0,13	4,32	**X2**	4,32	4,45	4,32	4,32	
1,7%	0,11	6,38	**X3**	6,38	6,38	6,49	6,38	
2,3%	0,07	2,99	**X4**	2,99	2,99	2,99	3,06	
4,2%	**0,024**	**0,557**	Result	0,562	0,574	0,548	0,544	
			diff	0,005	0,017	-0,009	-0,013	0,001

❽

index	3,7%	**50,8%**	16,1%	**29,4%**	100,0%
					sum

$$index = \frac{(y_i - y)^2}{\sum_i (y_i - y)^2}$$



Major Contributor :

- Type B? ☹
- Type A? ☺
- Replicates?
- Much work?
- Control Charts?

Slide 32

- 6 -
Use of
Reference Materials

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Use of
Reference materials

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Overview

- Definitions
- Types of RMs
- RM production
- Use of RMs
- CRM suppliers
- Examples on use

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Be aware!

What is presented here is best practice
on the use of reference materials
… in many cases this is not applied!

Quality Standards of preparation
are not systematically applied
by all suppliers

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Role of RM in Analytical Chemistry

ISO17025 (QA) requirements

- ✓ Suitable laboratory environment
- ✓ Educated, trained and skilled staff
- ✓ Suitable equipment
- ✓ Use of validated and documented methods
- ✓ Quality control
- ✓ Training procedures and records

- → Requirements for reagents, calibrants and measurement standards
- → Proper use of (certified) Reference Materials
- → Procedures for checking and reporting results
- → Proper storage and handling of samples
- → Participation in proficiency tests

Slide 4

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You certainly heard about...

✓Standards
- Primary and Secondary standard
- International (measurement) standard
- National standard
- Calibration standard
- Measurement standard

✓Reference Materials (CRM, SRM, ...)
- Primary and Secondary RM
- Laboratory RM
- Internal, "in-house" RM
- Matrix RM

+ Calibration solution
+ Control sample

Slide 5

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Definition of Reference Materials (RM)

According to VIM,

material or substance one or more of whose properties are sufficiently homogeneous and well established to be used for the calibration of an apparatus, the assessment of a measurement method, or for assigning values to materials

Slide 6

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Definition of Certified Reference Materials (CRM)

According to VIM,

reference material, accompanied by a certificate, one or more of whose property values are certified by a procedure which establishes traceability to an accurate realization of the unit in which the property values are expressed, and for which each certified value is accompanied by an uncertainty at a stated level of confidence

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Types of CRMs according to their use

- Pure substances for calibration
  (e.g. solution of Pb to prepare calibration solution for AAS)
- Pure substances for matrix matching
  (e.g. high purity Cu to make a Zn/Cu calibration series for ICP-ES)
- matrix CRMs
  (e.g. cholesterol in serum)

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Matrix RM

According to VIM,

Matrix (compositional) reference material :
A "natural" substance more representative of laboratory samples that has been chemically characterised for one or more elements, constituents etc. with a known uncertainty

Measurand

- Measurand: what you try to measure
- independent of measurement procedure
  (e.g. 'total Pb' content in a soil)
- dependent on the procedure,
  i.e. an operationally defined measurand
  (e.g. Pb content of a soil after aqua regia extraction at 80 ^{o}C for 24 h)

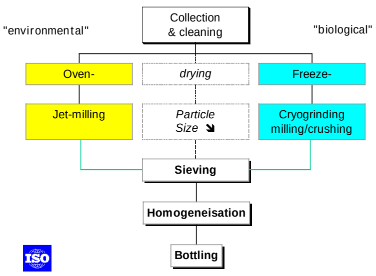
Making CRMs, not a trivial job !

- Know-How and infrastructure
  to process the material in a suitable form,
  specially for matrix CRMs
- Demonstrated measurement capability,
  to produce reference value

Example

Prepare 5000 bottles of a fish sample
for Hg content measurement,
with demonstrated homogeneity and stability

(C)RM production, not a trivial thing



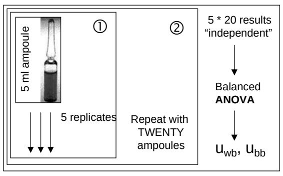
According to ISO 35 producing (C)RMs is ...

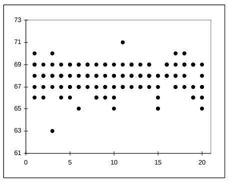
– the integrated process of correct preparation, homogeneity and stability <u>demonstration</u>, and accurate and traceable charaterisation,

– whereby all components of uncertainty of “*the sample on the desk of the user*” should be properly accounted for according to the ISO Guide Uncertainty of Measurements (GUM)

Homogeneity

of each element

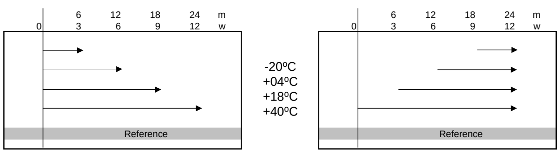




1. Homogeneity contribution to uncertainty

Stability

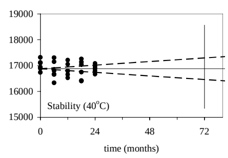
of each element



Classical | *Isochronous*

2. Stability contribution to CRM uncertainty & shelf-live

Measured under <u>repeatability</u> conditions



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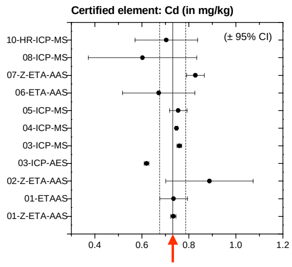
"Characterisation"
Value assignment

- ✓ *by designation*
- ✓ 1 method / 1 lab
- ✓ 1 method / M labs
- ✓ N methods / 1 lab
- ✓ N methods / M labs



3. Characterisation contribution to CRM uncertainty

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(C)RM Uncertainty
according to GUM

Expanded Uncertainty U_{CRM} of the average concentration of 1 unit after storage for (some) time and after transport

$$U_{CRM} = k \cdot \sqrt{u_{bb}^2 + u_{lts}^2 + u_{char}^2}$$

- k: Coverage factor
- u_{bb}: Between-Bottle
- u_{lts}: Long-term stability
- u_{char}: Characterization (Certification)

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A high quality (C)RM should :

- State traceability of certified value
  (e.g. traceability to S.I., or to values obtained with method XYZ)
- State an ISO-GUM uncertainty of certified value
- Demonstrate traceability & uncertainty of certified value
  (e.g. in a certification report ; experimental evidence of demonstrated capability from participation to international intercomparisons such as those from BIPM)
- Produced according to ISO-35 and ISO-34 (preferably)

OK, we can rely on (C)RMs

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How to handle CRMs ?

- Follow the “Instructions for use” given by the supplier
- Comply with the prescribed minimum sample intake
- Respect storage temperature (-20, +4, +18 ºC ?)
- Beware of humidity/moisture uptake (e.g. biological activity)
- Avoid contamination
- If method prescribed, apply protocol accordingly

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Use of CRMs ?

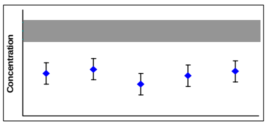
I use a CRM, therefore my measurement result is *automatically* correct
wrong

I use a CRM for:

✓ calibration inside a measurement procedure *(cf. solution standards)*

✓ validation of analytical procedure *(do I get the value given in the certificate, applying my experimental procedure ?)*

✓ input parameter in the model equation (*I.e. Recovery*)



Why is there a bias?
What is wrong with my procedure?

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Choose the proper CRM

- Is there a choice (similar matrix) ?
- What is your uncertainty requirement ?
- What is the uncertainty U_{CRM} ?
- Contribution of U_{CRM} on your measurement result
  (if digestion is 90% of uncertainty …) ?
- Traceability of CRM values ?
- CRM supplier with demonstrated capability ?
- Cost ?

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CRMs yes, but ...

- Is your procedure validated ?
- What about your Quality System ?
  (procedure, Lab, instruments, your staff, your organisational processes)
- Do you participate to Inter-Laboratory Comparisons ?

  - *Do NOT use CRMs as QC samples*
    use "in-house" materials or QC materials, instead
    (LRM, expired CRMs, etc…)

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How to find (C)RMs

The selection of appropriate CRM's by the user with respect to sample matrix, concentration range and uncertainty of certified properties is essential

Information and catalogues available on the web:

IRMM	*www.irmm.jrc.be*
BAM	*www.bam.de (& COMAR dbase)*
NIST	*www.nist.gov*
LGC	*www.lgc.co.uk*
others	…

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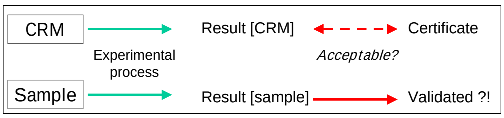
(C)RM no (C)RM ?

1) Solution standard, Pure substances
→ Calibration
→ "matrix matching" *(cf. water analysis)*
→ Spiking / standard addition
(cf. Example 1: MPA in lemonade)

2) "matrix" CRMs available
2.1 "matching"
(sediment sample; sediment CRM; similar concentration range)



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(C)RM no (C)RM ?
continued

2) "matrix" CRMs available
2.2 "similar"
(sediment sample; soil CRM; different concentration range)

same reasoning as in 2.1
BUT, do the two matrices behave the same throughout the whole experimental process ?
➔ measure other CRM for confirmation

3) no available (C)RM
– use different sample treatments
– use different experimental methods
– use ILC results
➔ compare results …/…

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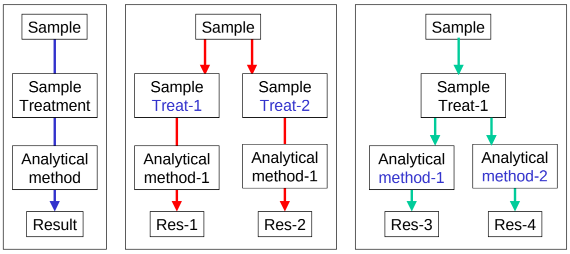
Use (C)RMs to estimate Uncertainties



Compare Results

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Matching - No Matching

Similar matrix AND similar analyte concentration

- Serum sample v.s. serum CRM
- steel v.s. steel CRM
- natural water v.s. water CRM

Similar matrix / different analyte concentration
different matrix / similar analyte concentration

- wine (country 1) v.s. wine (country 2) CRM
- river sediment v.s. calcareous soil CRM

➔ check for interferences

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Example 1
Pure substance

Recent Food Scare:

MPA* in Irish pharmaceutical sucrose waste, undeclared/illegal transport to Belgium

➔ ended up in human food!

Measurement problem / Measurand:

Total MPA content in lemonade [mg/kg]

CRM available:

pure MCA

**MPA = Medroxyprogesterone-acetate*

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Example 1
continued

Method:

- Procedure for MPA in human serum by GC-MS
  literature = [Choi et al. (2001)]
- Modify procedure to measure MPA in lemonade sample
- Use standard addition method
- Spike the sample with pure MPA
- Determine the MPA content in limonade.

❶ Validation required
❷ lemonade homogeneity
❸ spike homogeneity in lemonade
❹ spike and measurand behaviour in matrix
❺ pure substance traceability

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Example 2

Measurement problem:
Determine Cu and Fe content in paper,
at mg/g levels, with uncertainty of 10%.

- No international written standard procedure
- No *(matching)* paper CRM available

Suggested procedure:
sampling 0.8 g paper, microwave digestion…; dilution with HNO_3 (1 M)
- Measurement using ICP-MS; - Measurement range 0.1-100 ng/ml
- Possible spectral interferences
- Visual inspection of digested sample : complete digestion/no residues

❖ *"digested paper sample" matched by a water CRM*

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Some thinking

Identify (all possible) sources of uncertainty :

- dilution
- weighing
- contamination
- digestion - recovery
- spike homogeneity
- spike/measurand chemical form
- …

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Use CRMs when you can,
BUT use them properly

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1) Questions ?

2) Module Evaluation

- 7 -

Inter-Laboratory Comparisons

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Inter-Laboratory Comparisons (ILC) and Proficiency Testing (PT)

Slide 1

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Overview

- Definitions
- Types of ILCs
- Why to participate
- How ILC are organised
- Assignment of values & evaluation
- ILC organisers
- Corrective Action after participation

Slide 2

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Definitions

Inter-Laboratory Comparison - ILC
'Organisation, performance and evaluation of tests on the same or similar test items by two or more laboratories in accordance with predetermined conditions'

(Laboratory) Proficiency Testing - PT
'Determination of laboratory testing performance by means of inter-laboratory test comparisons'

[ISO/IEC Guide 43:1997]

Slide 3

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Goals of an ILC

- ILC to demonstrate competence and establish degree of equivalence between results of the participating laboratories
- ILC used to assign certified values to RMs
- ILC to standardise/improve a method
  (determine repeatability, reproducibility, ...)
- ILC as a training exercise to improve skills

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Why participate ?

'trust is nice, proof is better'

- To demonstrate your competence to
  - 'yourself' (inside your lab)
  - to your direct customer
  - to 3rd parties (e.g. accreditation)
- To improve measurement skills *(educational aspect)*

just a snapshot

According to the Guide for Accreditation Bodies (EN 45003:1995, § 6.8.1):
"Laboratories shall be encouraged by the accreditation bodies to participate in proficiency testing or other inter-laboratory comparisons"

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Organising PT/ILC (1)

I - Design

- Establish objectives/ purpose
- Selection of organiser
- Selection of sample/matrix & measurand/analyte
- Selection material provider
- Preparation of Test material
- Test of Homogeneity and stability
- Determination of assigned/reference value
- Selection of participants

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Organising PT / ILC (2)

II - Execution

- Distribution of test samples to participants
- Analysis by participants *(measurand quantification)*
- Reporting by participants to Organiser

III - Evaluation

- Evaluation of results
- Reporting by Organiser to participants *(feedback)*
- Draw Conclusions ➔ *corrective action*

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Performance Evaluation Criteria are set by the …

- Organiser of the PT/ILC
- Accreditation body
- Regulator
- Participating laboratories themselves

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How to obtain assigned values ?

- By formulation
- Value derived from
  - all participants results
  - a sub-set (after outlier rejection)
- Reference Value independent from participant results, with demonstrated *metrological quality*
  ➔ traceability and small uncertainty
  ➔ link to international measurement infrastructure

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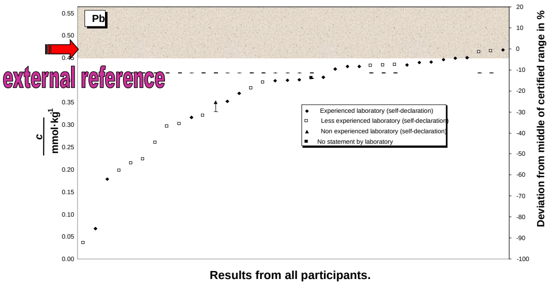
IMEP-13 : Metals in packaging waste
Pb in polyethylene (directive 94/62/EC)



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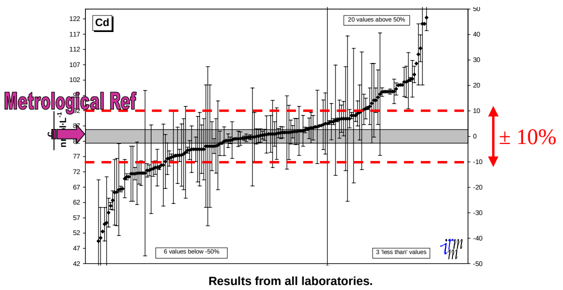
IMEP-9 : Trace Elements in Water



externally set deviation unit : set by legislation 98/83/EC

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Statistical treatment

- *Just a tool, not the key issue* !
  Use common sense and your technical experience !
- Depends on the type of ILC
- Needed in:
  - sample characterisation
  - data evaluation - treatment of results
  - performance evaluation

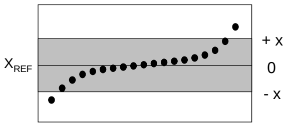
Slide 12

Performance Indicators

– Percent Error; $\%E = (x_{lab}-x_{ref})/x_{ref}$

– Z-scores; $Z = (x_{lab}-x_{ref})/s$

– En numbers; $En = (x_{lab}-x_{ref})/(u_{lab}^2+u_{ref}^2)^{½}$



Performance evaluation, P:
P ≤ x, Satisfactory
P > x, Unsatisfactory

See Module "Statistics"

ILC for method Validation

- Objective: determine procedure repeatability "s_r" and reproducibility "s_R"
- Evaluation using ANOVA (Analysis of Variance)
- Check for Outliers (before averaging/concluding)
  - – Cochran test for variance outliers,
  - – Grubbs test for average outliers

[ISO5725-2]

ILC for (C)RM certification

- Objective: determine the certified value and it's uncertainty for Reference Materials
- Uncertainty estimation, u_{char} (ISO-GUM)
- Technical Discussion Meeting

[BCR 1/97]

See Module "CRM"

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ILC for performance evaluation

- Objective: determine the performance of laboratories
- Evaluation Parameters:
  - Assigned value
  - Deviation unit
- Evaluation of single performance
- Evaluation of combined performance with composite scores

[ISO Guide 43 & ISO/DIS 13528]

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A real case example

IMEP

IMEP-16

Measurand = Pb
Matrix = Wine
Methods = (ET/GF)- AAS
ICP-MS, ICP-AES
Participants: 130
Experienced Labs: Y/N
With Quality Systems : Y/N
Accredited: Y/N

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I participate to ILC

Measurand & Matrix known

Lab Code = X
Country = ???
Instrumental Method: ####
Sample Treatment (digestion, extraction, …)
Calibration (int, ext, std addition)
Humidity correction (when applicable)

Uncertainty Budget?	☐ Y	☐ N
Experience in field?	☐ Y	☐ N
Prescribed method?	☐ Y	☐ N
Quality System?	☐ Y	☐ N
Accredited?	☐ Y	☐ N

I got:
[Pb] = (25.5 ± 1.6) µg/l (k=2)
How did I perform?

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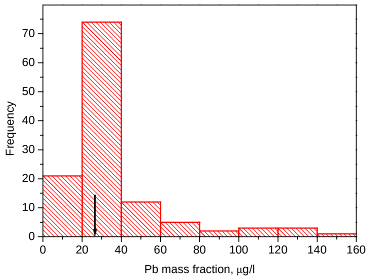
Distribution of results



Values ranging from "- 130" to "3000" (µg/l)

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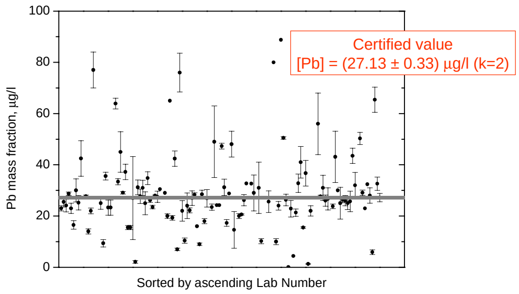
All the results (130)



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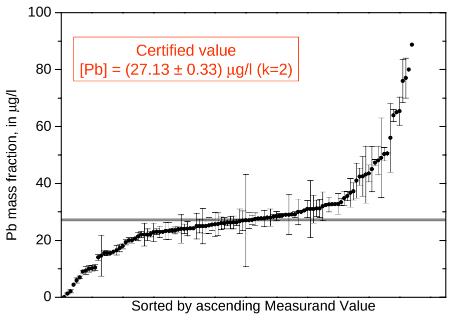
Graph à la IMEP



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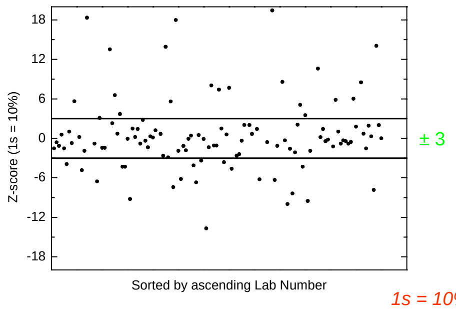
Data Evaluation
Z-scores



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How did I perform ?

	value	U (k=2)	u	RSu
ref	27.13	0.33	0.165	0.6%
lab	25.5	1.6	0.8	3.1%
		Expanded	*Combined*	

%E = **6%**
Z = **9.9**
En = **2.0** passed

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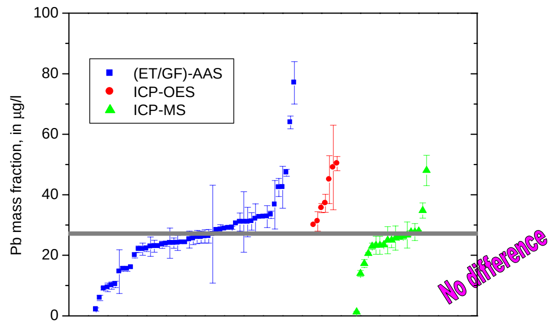
Preferred experimental method ?



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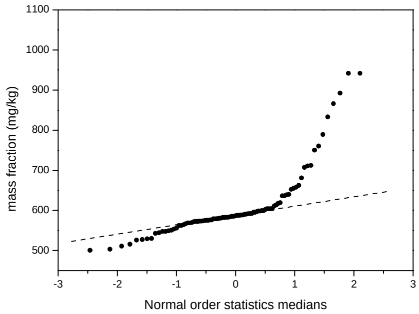
Normality Plot



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Corrective Action after participation :

1) 'blunder'
(measurement system out of control, calculation error)
2) Measurement 'model' is not correct : the mathematical description of reality is not complete enough,
(e.g. bias not taken into account: digestion? extraction?)
3) Underestimated uncertainty of an influencing input quantity
4) Combination of 2) and 3)

Unsatisfactory performance? ➔ Spot the mistake & implement Corrective Action

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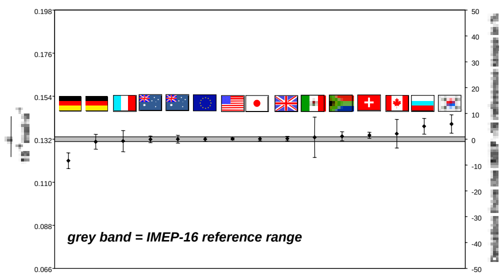
Solid External References in CCQM-P16



Results from all CCQM-P16 participants

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Who organises ILC/PT ?

- CCQM (www.bipm.fr)
- IMEP by IRMM (www.imep.ws)
  - external reference value, linked to international measurement capability
  - support to EA (European Cooperation Accreditation)
  - on issues related to EU directives, crossing borders of sectors & geographic regions
- FAPAS (www.fapas.com)
- AFSSA (www.afssa.fr)
- EA (www.european-accreditation.org)
- Community Reference Laboratories (CRLs), for National Reference Laboratories (NRLs)
- Other ➔ check www.eptis.bam.de
  (European Information System on PT Schemes)

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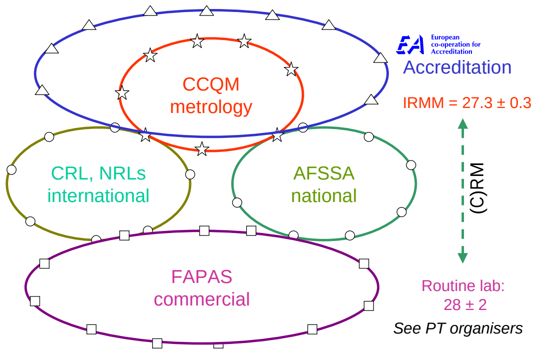
International measurement equivalence



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1) Questions ?

2) Module Evaluation

List of Abbreviations

AFSSA	Agence Française de Sécurité Sanitaire des Aliments
	French Food Safety Agency
APLAC	Asia Pacific Laboratory Accreditation Cooperation
APMP	Asia-Pacific Metrology Programme
BIPM	Bureau International des Poids et Mesures
	International Bureau for Weights and Measures
CCQM	Consultative Committee for Amount of Substance
CEN	Comité Européen de Normalisation
	European Committee for Standardization
CGPM	Conférence Générale des Poids et Mesures
	General Conference on Weights and Measures
CIPM	Comité International des Poids et Mesures
	International Committee for Weights and Measures
EA	European Accreditation
EUROMET	European Collaboration in Measurement Standards
FAPAS	Food Analysis Performance Assessment Scheme
GUM	Guide to Expression of Uncertainty in Measurement
ILAC	International Laboratory Accreditation Cooperation
ISO	International Organization for Standardization
IUPAC	International Union for Pure and Applied Chemistry
OIML	International Organisation for Legal Metrology
MRA	Mutual Recognition Arrangement
SIM	Inter-American Metrology System
VIM	International Vocabulary of Basic and General Terms in Metrology

Glossary

EUR 20841 EN

	Definitions
Accuracy of measurement	Closeness of the agreement between the result of a measurement and a true value of the measurand [VIM 3.5]
Calibration	Set of operations that establish, under specified conditions, the relationship between values of quantities indicated by a measuring instrument or measuring system, or values represented by a material measure or a reference materials, and the corresponding values realized by standards [VIM 6.11]
Certified Reference Materials	Reference Materials, accompanied by a certificate, one or more of whose property values are certified by a procedure which establishes traceability to an accurate realization of the unit in which the property values are expressed, and for which each certified value is accompanied by an uncertainty at a stated level of confidence [VIM 6.14]
Expanded uncertainty	Quantity defining an interval about the result of a measurement that may be expected to encompass a large fraction of the distribution of values that could reasonably be attributed to the measurand
International (measurement) standard	Standard recognized by an international agreement to serve internationally as the basis for assigning values to other standards of the quantity concerned [VIM 6.2]
Measurand	Particular quantity subject to measurement [VIM 2.1]
Measurement	Set of operations having the object of determining a value of a quantity [VIM 2.1]
Measurement procedure	Set of operations, described specifically, used in the performance of particular measurements according to a given method [VIM 2.5]
Measurement standard (etalon)	Material measure, measuring instrument, reference material or measuring system intended to define, realize, conserve or reproduce a unit or one more values of a quantity to serve as a reference [VIM 6.1]
Method of measurement	Logical sequence of operations, described generically, used in the performance of measurements [VIM 2.4]
Metrology	Science of measurement - Metrology includes all aspects both theoretical and practical with reference to measurements, whatever their uncertainty, and whatever fields of science or technology they occur [VIM 2.2]
Model equation	The equation used to calculate the result of a measurement
National(measurement) standard	Standard recognized by a national decision to serve, in a country, as the basis for assigning values to other standards of the quantity concerned [VIM 6.3]
Primary method	A method of the highest metrological quality which when implemented can be described and understood completely, and for which a complete uncertainty budget can be provided in SI units, the results of which can therefore be accepted without reference to a standard for the magnitude being measured.

	Definitions
Primary standard	Standard that is designated or widely acknowledged as having the highest metrological quantities and whose value is accepted without reference to other standards of the same quantity [VIM 6.4]
Quantity	Attribute of a phenomenon, body or substance that may be distinguished qualitatively and determined quantitatively [VIM 1.1]
Reference Material	Material or substance one or more of whose property values are sufficiently homogeneous and well established to be used for the calibration of an apparatus, the assessment of a measurement method, or for assigning values to materials [VIM 6.13]
Repeatability (of results of measurements)	Closeness of the agreement between the results of successive measurements of the same measurand carried out under the same conditions of measurement [VIM 3.6]
Reproducibility (of results of measurements)	Closeness of the agreement between the results of measurements of the same measurand carried out under changed conditions of measurement [VIM 3.7]
Result of a measurement	Value attributed to a measurand, obtained by measurement [VIM 3.1]
SI system	The international system of unit continuing the formal definition of all SI basic units, approved by the General Conference on Weights and Measures
Standard uncertainty	Uncertainty of the results of a measurement expressed as a standard deviation
Traceability	Property of result of a measurement or the value of a standard whereby it can be related to stated references, usually national or international standards, through an unbroken chain of comparisons all having stated uncertainties [VIM 6.10]
True value (of a quantity)	Value consistent with the definition of a given particular quantity [VIM 1.19]
Uncertainty of measurement	Parameter, associated with the result of a measurement, that characterizes the dispersion of the values that could reasonably be attributed to the measurand [VIM 3.9]
Unit (of measurement)	Particular quantity defined and adopted by convention, with which other quantities of the same kind are compared in order to express their magnitudes relative to that quantity.
Value (of a quantity)	Magnitude of a particular quantity generally expressed as a unit of measurement multiplied by a number [VIM 1.18]

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Abstract

A common understanding of issues related to measurement science applied to chemistry is essential among European member states and acceding- candidate countries. An education platform was therefore created to respond to this challenge: TrainMiC, Training in Metrology in Chemistry.

After a brief presentation of TrainMiC and an overview of TrainMiC events, this report provides the complete set of the training material. The seven modules are included in the Appendix.

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