Measurement Uncertainty – Principles and Implementation in QC

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About Measurement Uncertainty

Have you heard this one before ?

A bus has 10 people in it and stops at a bus stop.

11 people get off.

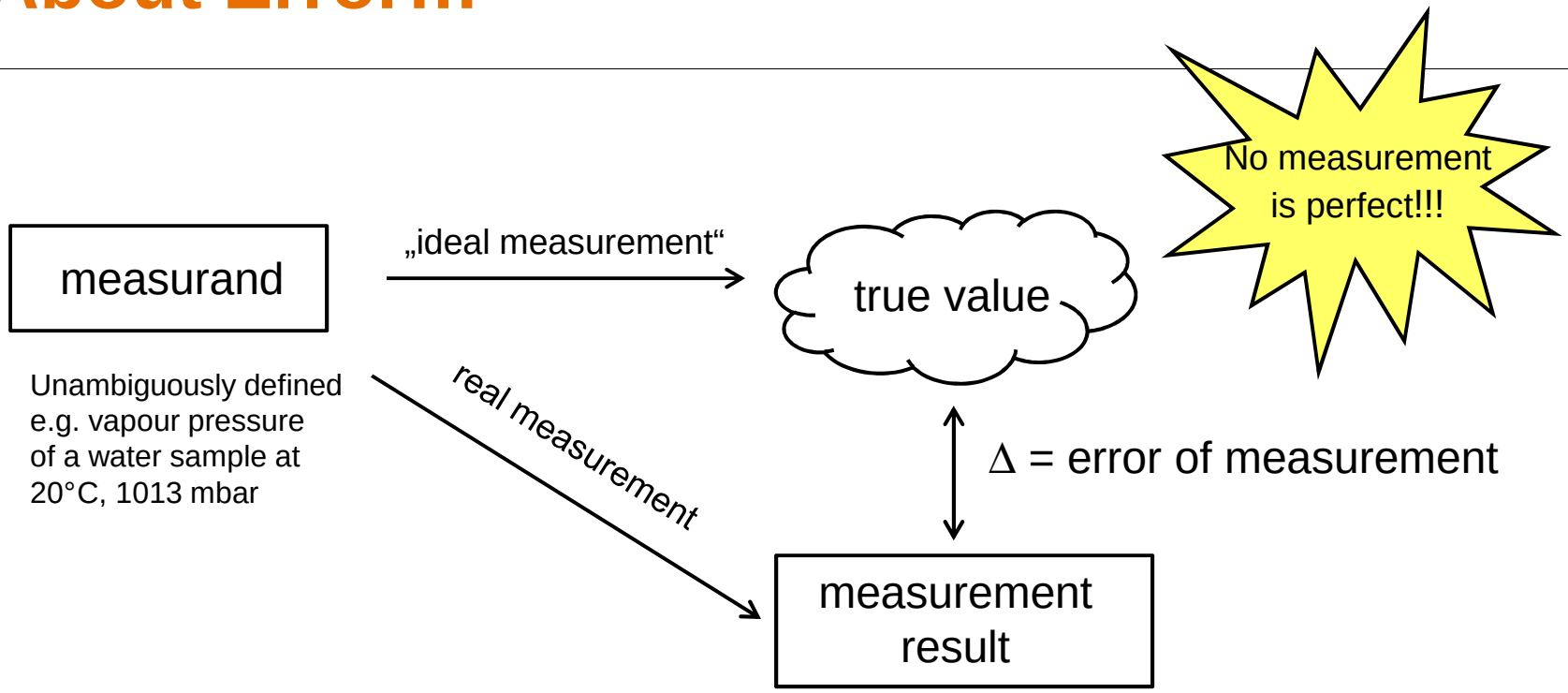
3 scientists comment as follows:

The biologist: **„They must have reproduced during the journey.“**

The mathematician: **„If somebody else gets on, there‘ll be nobody left on the bus.“**

The analyst: **„What the hell; you have to expect 10 % measurement uncertainty!“**

About Error…



Definition of uncertainty of measurement (ISO Guide to the expression of uncertainty in measurement, GUM)

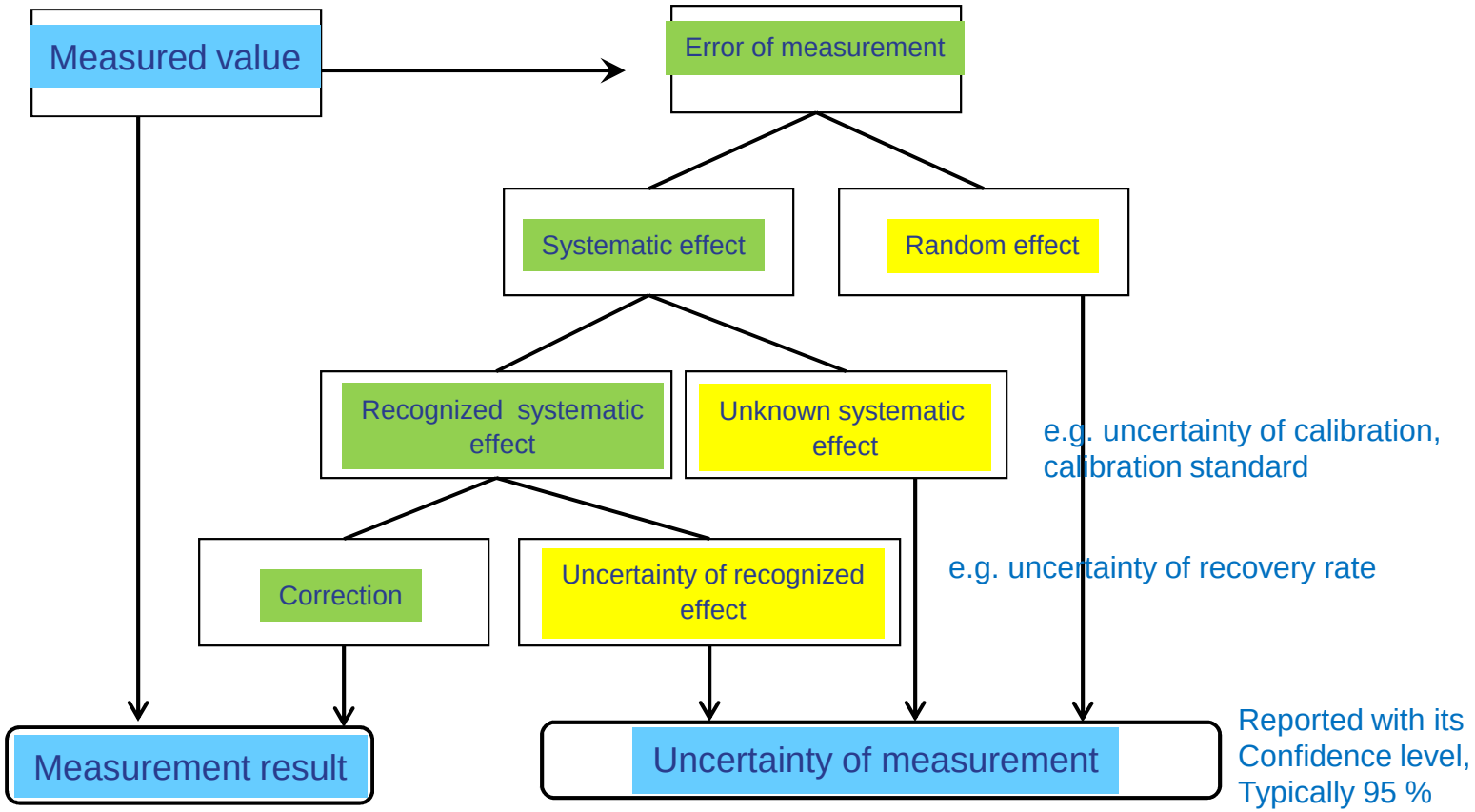
uncertainty of measurement

Parameter, associated with the result of a measurement, that characterizes the dispersion of the values that could reasonably be attributed to the measurand

The uncertainty of the result of a measurement reflects the lack of exact knowledge of the value of the measurand. Traditionally, uncertainty of measurement consists of two components: a random and a systematic component.
Random error (arising from unpredictable or stochastic temporal and spatial variations of influence quantities) gives rise to variations in repeated observations of the measurand (note: cannot be eliminated but usually can be reduced by increasing the number of observations)
Systematic error cannot be eliminated too, but often can be reduced (remark: and should/must be reduced) by correction if the systematic effect can be quantified appropriately.

The result of a measurement after correction for recognized systematic effects is still only an estimate of the value of the measurand because of the uncertainty arising from random effects and from imperfect correction of the the result for systematic effects.

Error / Uncertainty of measurement



Uncertainty of measurement is typically (due to lack of time and resources) determined by estimation and therefore is itself an estimated value

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ISO 17025 Uncertainty of measurement

5.4.6.2

Testing laboratories shall have and shall apply procedures for estimating uncertainty of measurement.

In certain cases the nature of the test method may preclude rigorous, metrologically and statistically valid calculation of uncertainty of measurement. In these cases the laboratory shall at least attempt to identify all components of uncertainty and make a reasonable estimation, and shall ensure that the form of reporting of the result does not give a wrong impression of the uncertainty.

Reasonable estimation shall be based on knowledge of the performance of the method and on the method scope and shall make use of, for example, previous experience and validation data.

ISO 17025 Test reports

5.10.3.1

In addition to the requirements listed in 5.10.3, test reports shall, where necessary for the interpretation of the test results, include the following:

a) ...

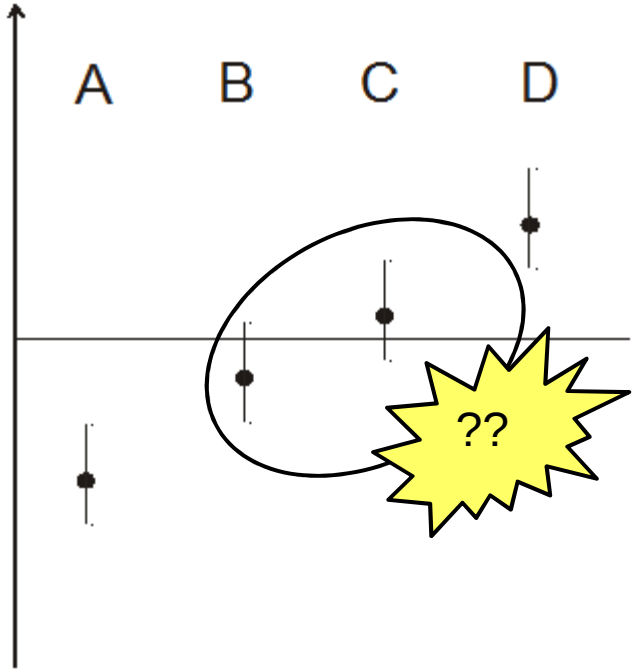
b) ...

c) **where applicable, a statement on the estimated uncertainty of measurement; information on uncertainty is needed when it is relevant**

- **to the validity or applicability of the test results,**
- **when a client‘s instruction so requires**
- **or when the uncertainty affects compliance to a specification limit**

Who needs uncertainty of measurement

- The customer to assess the quality of a test result
- The laboratory to assess whether a limit (e.g. specification limit) is maintained or not ⇒ questions of liability
- The laboratory to decide whether a method principle is applicable or not
- Both, the laboratory and/or the customer in order to compare two measurement results with respect to equivalency
- Important Remark: Uncertainty of measurement is not applicable to compare laboratories !



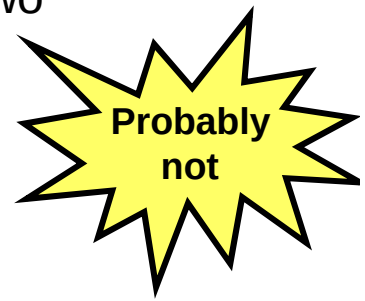
Unequivocally in-spec

Limit

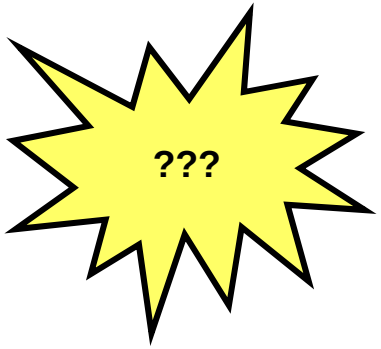
Unequivocally off-spec

Example for comparison of results

- The assay of Aflatoxin B1 in nuts via HPLC was determined in two laboratories
- 1st question: will both laboratories get identical results ?



- 2nd question: will both laboratories get comparable results
- Result lab 1: 3,0 ppb; Result lab 2: 2,7 ppb



- 3rd question: are the above results comparable ?
- Complete result lab 1: 3,0 ± 0,5 ppb
- Complete result lab 2: 2,7 ± 0,4 ppb
- 4th question: are the above complete results comparable ?

Literature:
A. Maroto, R. Boqué, Y. Vander Heyden, LC-GC, Europe, Dec. 2008

Reporting of test results with uncertainty of measurement

Example: Test result of a determination of aluminium

Assay of Al: 325 mg/kg ? How big is the dispersion ?

Assay of Al: 325 mg/kg ± 15 mg/kg ? How reliable is the dispersion ?

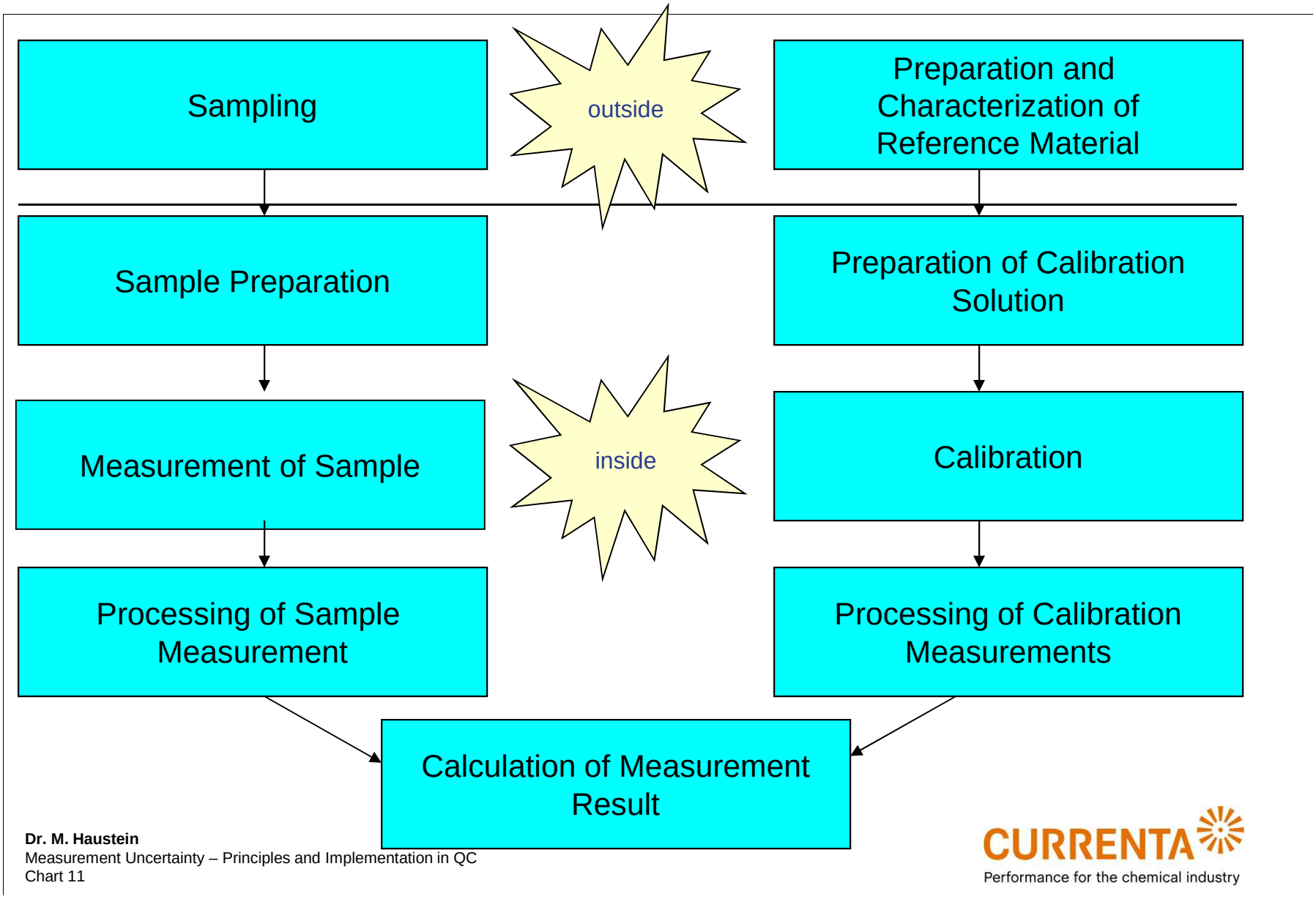
Assay of Al: 325 mg/kg ± 15 mg/kg (95%) (325 ± 15) mg/kg (95%)

A complete reporting contains:

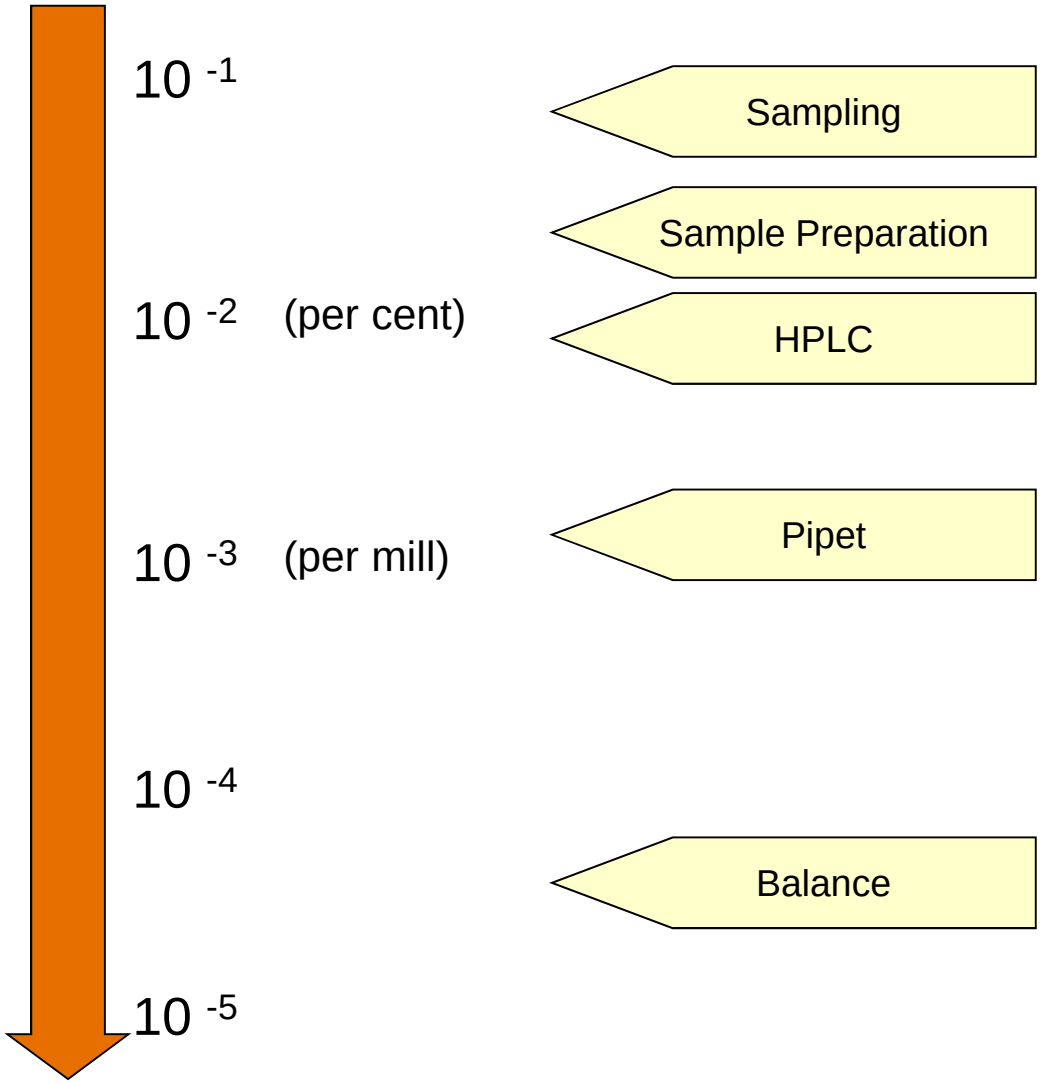
- Measurement result with unit
- Uncertainty with unit
- Confidence level

In Detail:
The uncertainty of measurement corresponds to the expanded uncertainty and was calculated with a coverage factor of k = 2 and corresponds to a confidence level of 95 %

Contributions to measurement uncertainty



Dimensions of measurement uncertainty



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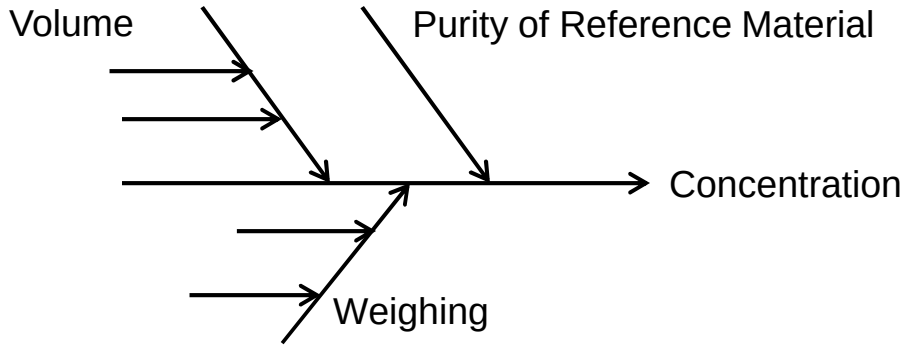
Determination of measurement uncertainty from individual uncertainty contributions (GUM) [1]

According to Eurachem/CITAC-guideline [1)] „Quantifying Uncertainty in Analytical Measurement“ (2nd edition, 2000):

1)Application of the concepts of the ISO Guide (GUM) to chemical measurements

- Specification of Measurand / Calculation of Result (Formula)

- Identification of uncertainty sources („cause and effect“-diagram*)



- Measurement (type A) or estimation (type B) of the individual uncertainty components
- Calculation of combined uncertainty u_c via error propagation or addition of variances

* fish-bone- or Ishikawa-diagram

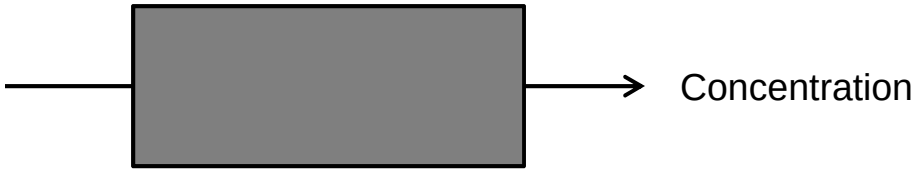
Determination of measurement uncertainty [1] – Pros and cons

- Pro
  - „white-box“
    Individual uncertainty sources and their contributions are known in detail
- Con
  - Generally very time-consuming, complex and expensive as one has to identify/quantify each individual contributions
- Consequence
    - Typically not applied in routine !

Determination of measurement uncertainty by using experimentally determined quality control and method validation data (NORDTEST)

Use of standard deviations from precision-/accuracy experiments or data from external or internal quality control, e.g.

- Data from collaborative trials
- Data from control charts
- Calibration data



Con:
No information about individual uncertainty sources and their contributions („black-box“)
Pro:
Data are generally available, therefore no additional effort

Measurement uncertainty in quality control lab – Estimation from validation data

- Random effects:

  Marginal note:
  The determination of the random effects should be reasonably performed under these conditions which occur when the method is routinely applied during day-to-day business, that means data should be derived from day-to-day measurements (not measured at only one day !) and in addition using different apparatus and from different operators. These conditions are neither repeatability nore reproducibility conditions and therefore are called within-laboratory reproducibility conditions (alternative: intermediate precision)

  - By use of measurement values from representative control samples (with matrix !)

    If there are data from periodical measurements of a representative control sample available and covers the control sample the whole analytical process, then the random effect can be directly derived from the standard deviation of these data, e.g. from a control chart

Measurement uncertainty in quality control lab – Estimation from validation data

- From Validation data (e.g. precision)

  marginal note:
  no data from control charts are available may be due to instability of control sample or due to the lack of sufficient amount.
  Only repeatability data available (problem: repeatability does not contain dispersion effects of different apparatus and/or different operators and therefore does not represent typical standard deviation of the day-to-day business)

  Estimation of the random effect by multiplication of the repeatability standard deviation with a factor 1.5 – 2.
  (factor refers to the results of Horwitz reporting a ratio of approx. 1.5 between repeatability and reproducibility results; factor compensates „lack“ of dispersion of repeatability data)

Measurement uncertainty in quality control lab – Estimation from validation data

- Systematic effects

Marginal note:
According to GUM a measurement value has to be corrected for all recognized significant effects and every effort has to be made to identify such effects.
The estimation of the systematic effect principally is based on:

- the systematic deviation itself (difference (in percentage) from conventional true value or from certified value)
- the uncertainty of the conventional true or certified value, respectively

- Measurement of Certified Reference Materials (CRM's, quantified through a certification process (traceable to SI-unit and with a known uncertainty)

  The reference material should be analysed in at least 5 differential analytical series (e.g. on 5 different days) before the values are used.

- Calculation of the systematic effect according to the formula below:

$$u(bias) = \sqrt{(bias)^2 + \left(\frac{s_{bias}}{\sqrt{n}}\right)^2 + u(Cref)^2}$$

u(bias) = systematic effect
bias = difference between mean measured value and certified value
s(bias) = standard deviations of the CRM-measurements
√n = no. of measurements
u(Cref) = uncertainty from the certified value

Measurement uncertainty in quality control lab – Estimation from validation data

- Combined measurement uncertainty

  After determination/estimation of random effects and systematic effects in the next step both are combined via an addition of variances yielding the combined uncertainty (see formula below)

$$u_c = \sqrt{u(R_w)^2 + (u(bias))^2}$$

u_c = combined uncertainty
u(bias) = systematic effect
$u(R_w)$ = random effect

- Final Remark

  The contribution of the systematic effect is often insignificant compared to the random effect. This is valid, if serious errors, e.g. like inaccurate declaration of reference material can be excluded.
  Therefore, a simple but acceptable estimation of measurement uncertainty can be derived by reduction to the term of random effects.

Measurement uncertainty - terms

standard uncertainty „u“

Uncertainty of the result of the measurement expressed as a (single) standard deviation

combined (standard) uncertainty „u_c“

Combination of a number of standard uncertainties (via error propagation, simplified: via addition of variances (taking the square root of the sum of the squares) if standard uncertainties are stochastically independent)

expanded uncertainty „U“

Calculated from the combined (standard) uncertainty by multiplication with a coverage factor k (typically: k = 2) providing a level of confidence of approximately 95 %

Addtion of Variances – combined uncertainty

Two methods shall be compared with respect to the individual dispersion. The individual effects are known.

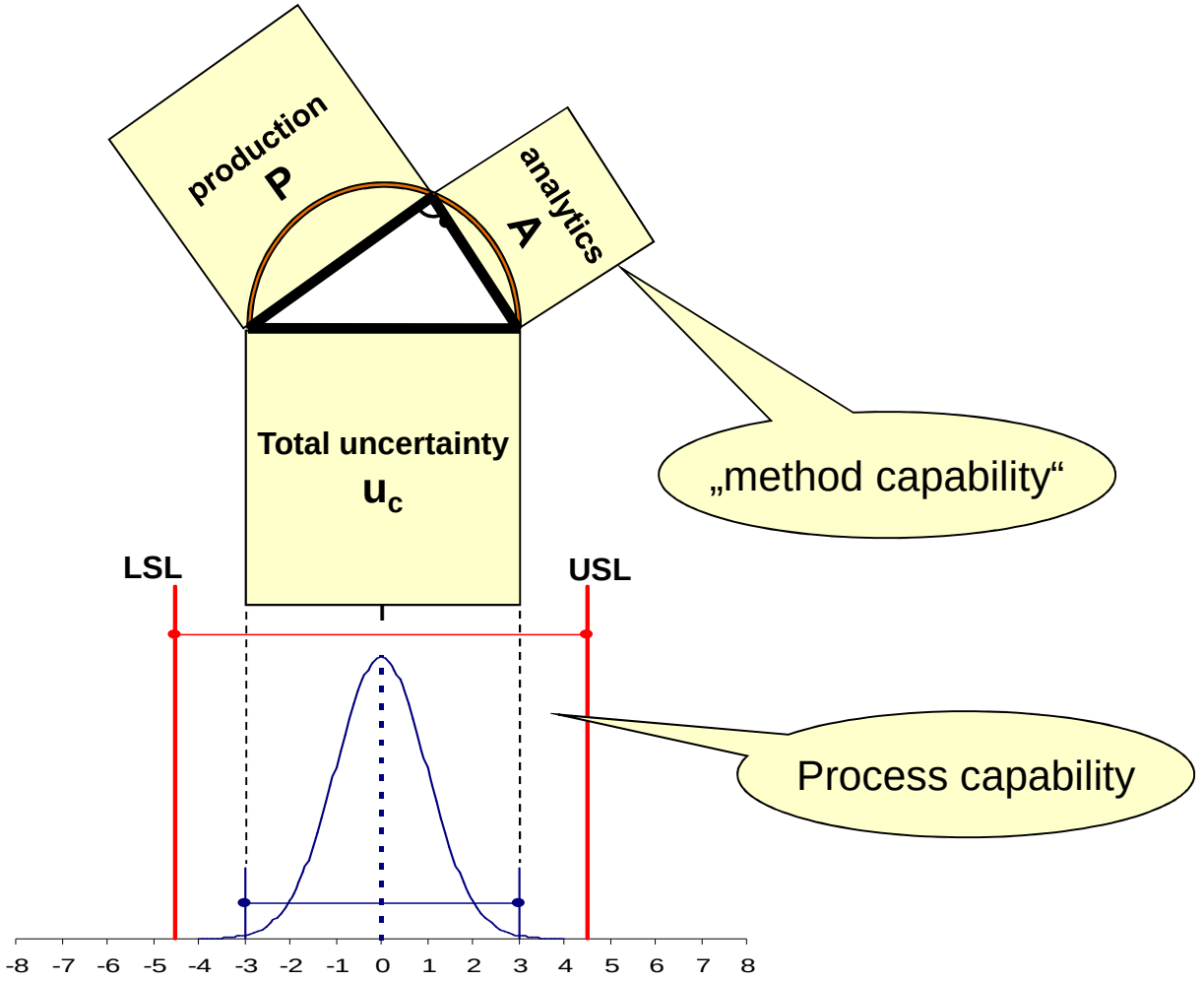
Which one is the better one?

	Method 1		Method 2	
	s	s^2	s	s^2
Sampling	3	9	7	49
Sample Preparation	3	9	1	1
Measurement	3	9	1	1
Total	5,2	27	7,1	51

Method 2 is dominated by the sampling procedure. The other effects are small and yield only small contributions to the total dispersion

In general: contributions which are significant (factor 5-10) below other contributions are negligible !

Addition of Variances – process cabability



Determination of combined uncertainty

Example : **Assay determination of an Aldehyde**

Step 1: Specification of Measurand / Calculation

Assay of Aldehyde in %, GC area percent method minus corresponding acid from titration

Step 2: Identification of the uncertainty components

1.	Sampling:	homogeneous liquid
2.	Stability of product (aldehyde):	oxidation during sampling (formation of acid with oxygen)
3.	Determination of acid:	standard deviation of titration
4.	GC-determination:	standard deviation of chromatography

Step 3: Testing schedule

Sampling:	6 independent samples out of 1 container within one day; Repeatability conditions in order to minimize dispersion of analyses (GC, Titr.)
Stability of product:	6-fold determination of 1 sample within several days; see above
Acid determination:	1 Sample, 6 operators, 6 days (within-laboratory reproducibilty)
GC-determination:	1 Sample, 6 operators, 6 days (within-laboratory reproducibilty)

Determination of combined uncertainty

Step 4: Evaluation of uncertainty for assay of Aldehyde

Measurement result GC: 99,37 %

Measurement result Titration: 0,22 %

Measurement result Aldehyde: 99,15 %

Complete measurement result: (99,15 ± 0,14) % (P = 95 %)

Source	Standard deviation	Variance
Sampling		
GC-determination	**0,018**	**0,000324**
Acid titration	**0,009**	**0,000081**
Product stability		
GC-determination	**0,018**	**0,000324**
Acid titration	**0,007**	**0,000049**
GC-determination (measurement)	**0,046**	**0,002116**
Acid titration (measurement)	**0,048**	**0,002304**
Combined uncertainty (GC)	**0,053**	**0,002764**
Combined uncertainty´(Titration)	**0,049**	**0,002434**
Combined uncertainty (total)	**0,072**	
Coverage factor k	**2**	
Expanded uncertainty	0,144	

Tips and Rules

- Multiply the easily accessible repeatability standard deviation with a factor of approx. 2 in order to obtain the reproducibility standard deviation as a realistic estimation for the random effect of the measurement uncertainty.
- Data from quality control charts should be preferred to validation data, as the prior data contain the dispersion of the day-to-day business and therefore are more realistic.
- Use standard deviations cited in standard documents (e.g. ISO norms) or from literature, if available
- Identify the 1-3 main uncertainty sources. Don‘t take too much effort to evaluate small uncertainty contributions, as they have almost no effect to combined uncertainty due to addition of variances. Focus on the main uncertainty sources in order to improve the measurement procedure,
- Take the complete analytical process into account namely from sample arrival up to the test report and don‘t focus only on the measurement itself as main uncertainty sources are typically found outside of the measurement, e.g. during sample preparation.
- Don‘t forget the sampling, even if sampling is not directly part of the measurement. Typically, sampling yields the main effect for the uncertainty.
- Ensure, that analytical data in test reports do not contain more digits than justifiable according to the accuracy of method. This is especially important if data are reported without measurement uncertainty.

Literature

- ISO/IEC guide 98-3:2008, *Guide to the Expression of Uncertainty in Measurement*, ISO, Genf (2008)

- EURACHEM/CITAC guide cg 4, *Quantifying Uncertainty in Analytical Measurement (QUAM)*, 2nd edition, 2000

- Nordtest Report TR 537, Edition 2 (2004*), Handbook for Calculation of Measurement Uncertainty in Environmental Laboratories*

- DEV, Deutsche Einheitsverfahren zur Wasser- , Abwasser- und Schlammuntersuchung, 64. Lieferung (2006), herausgegeben von der wasserchemischen Gesellschaft – Fachgruppe in der Gesellschaft Deutscher Chemiker mit dem Normenausschuss Wasserwesen (NAW) im DIN Deutsches Institut für Normung e.V.