Analytical error and uncertainty estimation

Ivo Leito
ivo.leito@ut.ee

https://analytical.chem.ut.ee/metals_ocean_2024/

University of Tartu

Main aims

- **The main aim:**
  - present a **practical approach** for **measurement uncertainty (MU) estimation**

- **Learning outcomes:**
  - Understanding
    - What is MU
    - What data are needed for MU estimation
  - Ability to
    - Critically evaluate the suitability of data
    - Perform MU estimation using the „top down“ approach
    - Present measurement results with uncertainty

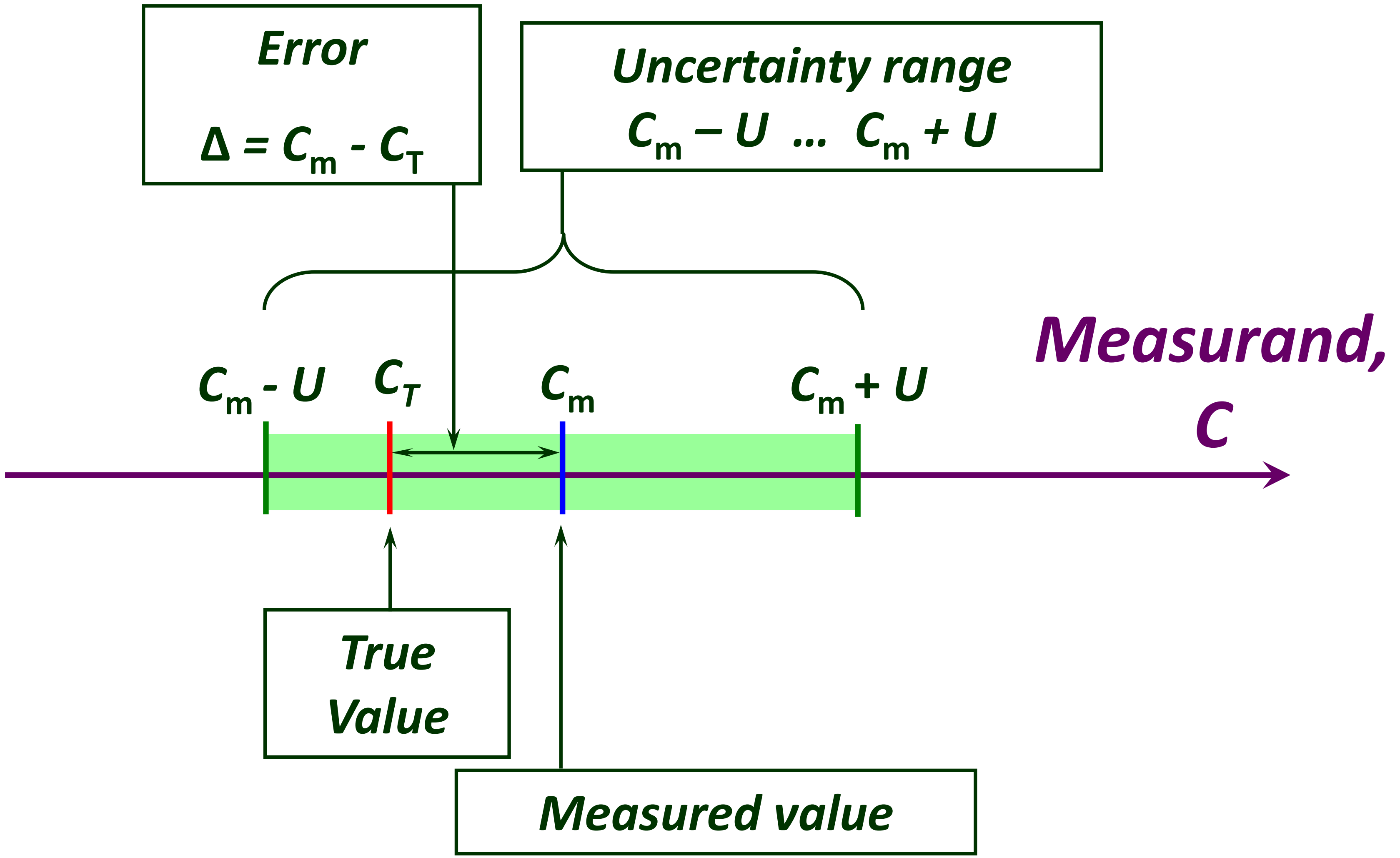
How we work

- **Practical applicability is more important than full rigor**
  - We simplify a lot
    - Occasionally close to the borderline of correctness
  - Only minimum of mathematics

- **Ask questions at any moment**

- You can freely distribute these slides

What are error and uncertainty?



Simplified definitions:

Error is the difference between the measured value (C_m) and the true value (C_T)

Uncertainty (U) is the half-width of a range around measured value (C_m) within which the true (C_T) value lies with a high probability

The probability is called **coverage probability**

What influences measurement result?

Random effects

Influence on measurement result:

- Cause **scatter**
  - in random direction
  - with random magnitude

Examples?

Systematic effects

Influence on measurement result:

- Cause **bias**
  - in the same direction
  - with constant (or proportional) magnitude

Examples?

Collectively: **Uncertainty sources**

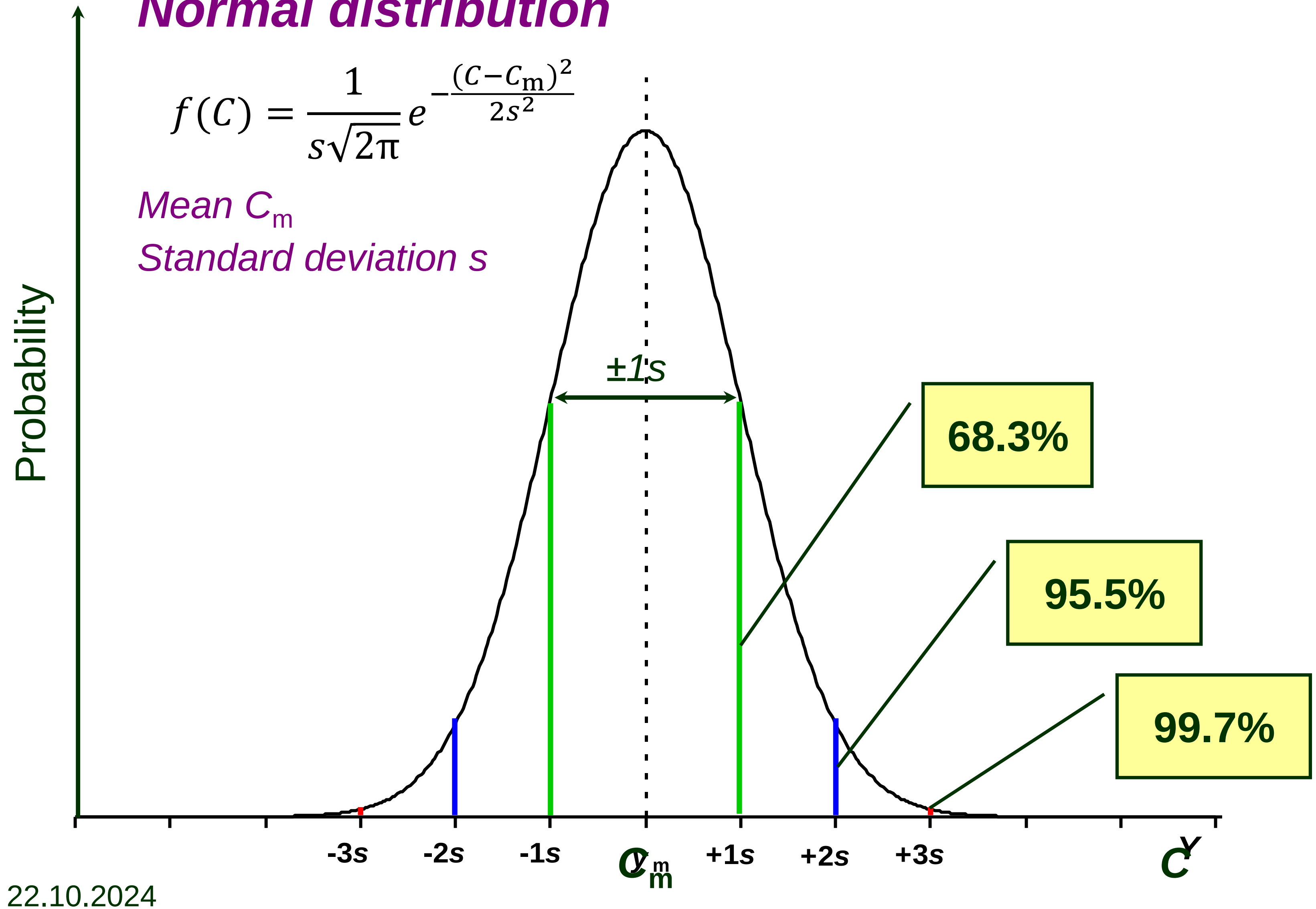
What about the probability?

Normal distribution

$$f(C) = \frac{1}{s\sqrt{2\pi}} e^{-\frac{(C-C_{\mathrm{m}})^2}{2s^2}}$$

Mean C_{m}

Standard deviation s



Simplified definitions:

Standard uncertainty (u, u_c): uncertainty expressed as standard deviation, i.e. with coverage proability ≈68%

Expanded uncertainty (at k = 2 level) (U): uncertainty with coverage proability ≈95%

The main question of uncertainty evaluation in an analytical lab:

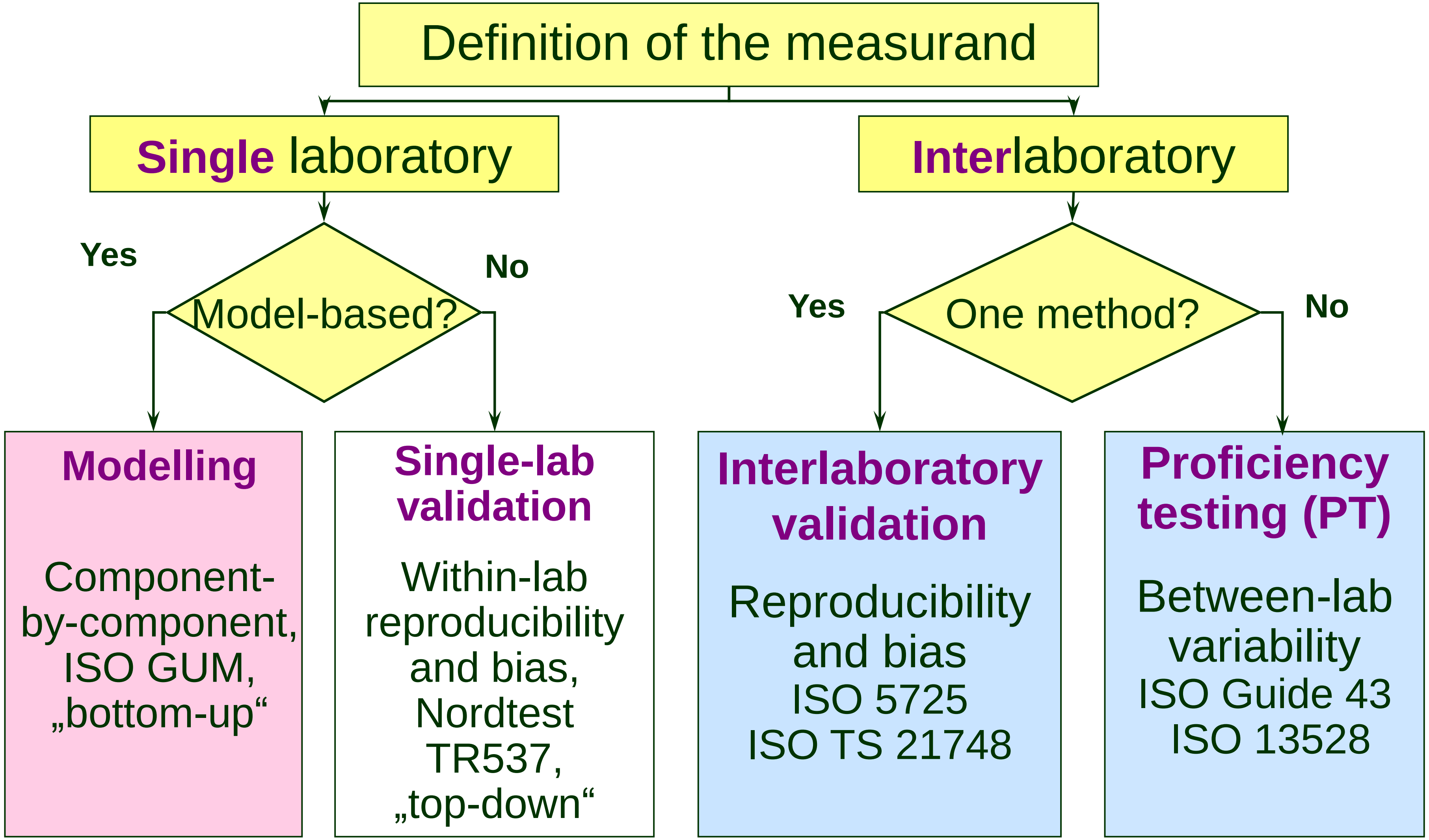
The uncertainty sources are more or less known

There are different data available (control charts, PT results, parallel measurements …)

How to use these data to take these uncertainty sources into account?

Different approaches offer different solutions to this question

Uncertainty estimations approaches



Eurolab Technical Report No 1/2007 Available from: http://www.eurolab.org/

Which approach should I use?

- If you have
  - Competence and time
  - Data on all important influencing quantities
    - Use the Modelling approach
      - If you omit something: underestimated uncertainty!

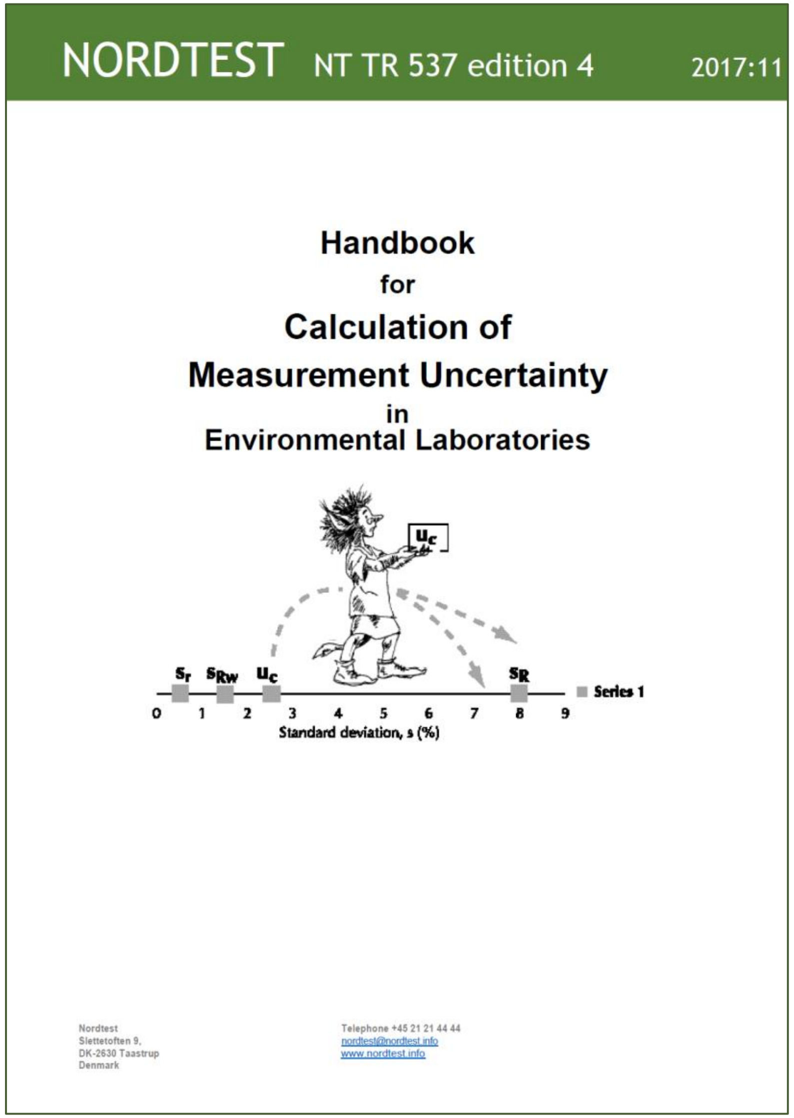
- If you have
  - Quality control data and results of participation in ILC-s or CRM analysis
    - **Use the Single-lab validation approach**
    - **In this course we use only this approach**

- Interlab approaches are not generally recommended
    - Use only if you do not do that measurement in your lab

„Single-lab validation“ approach

aka “the Nordtest approach„

based on validation and Quality Control Data



Nordtest Technical Report 537, ed 4 (2017)
http://www.nordtest.info/

Single-laboratory validation approach

Effects contributing to uncertainty

Random | **Systematic**

- The two groups of uncertainty contributions are quantified separately and then combined:

$$u_c = \sqrt{u_1^2 + u_2^2}$$

Uncertainty arising from random effects | **Uncertainty accounting for *possible* bias**

Simplified definitions:

Bias: estimate of systematic error.

Bias can be obtained as difference between the mean of a number of measurements with a reference sample and the respective reference value

Long-term!

Systematic and random effects

- *Random and systematic effects can be grouped differently:*

Short-term: *Within-day bias* | *Repeatability s_r*

Long-term: *Long-term bias* | *Intermediate precision s_{RW}*

(lab and method bias)

All effects causing error/uncertainty

Nordtest approach operates in the „long-term“ mode!

The longer is the time frame the more effects change their „status“: systematic → random

Examples?

Single lab validation approach: in practice

- The main equation:

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

Within-laboratory reproducibility

This component accounts for the long-term random effects

Uncertainty of the estimate of the possible laboratory bias and the possible method bias

This component accounts for the possible long-term systematic effects

- This and subsequent equations work with absolute and relative values

Nordtest Technical Report 537, ed 4 (2017)
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Meaning of the Nordtest uncertainty estimate

- The data used in Nordtest uncertainty estimation are **not directly related** to the specific result obtained on a specific day

- Therefore:

1. the obtained uncertainty is an **average uncertainty** of the method
2. and is **assigned** to the result

Absolute vs relative uncertainties

- Analyte concentration in today's sample is diferent from the data used for uncertainty estimation
- This brings in the question:
  - **Should we use absolute or relative uncertainties?**

- In general, **use whichever stays more constant** when the analyte concentration changes

- In addition:
  - **At low concentrations** (near detection limit, trace level) or if the concentration range is narrow, **use absolute uncertainties**
    - Uncertainty is not much dependent on analyte level

  - **At medium** and high concentrations **use relative uncertainties**
    - Uncertainty is roughly proportional to analyte level

Single lab validation approach: in practice

Steps:

1. Specify measurand
2. Quantify within-lab reproducibility component $\boldsymbol{u(R_w)}$
3. Quantify bias component $\boldsymbol{u(bias)}$
4. Calculate combined standard uncertainty $\boldsymbol{u}_c$
5. Calculate expanded uncertainty $\boldsymbol{U}$

The obtained uncertanty is **average uncertainty** of the method and is **assigned** to the result

- $u(R_w)$ is the uncertainty component that takes into account long-term variation of results of the same sample within lab
  - that means: **within-lab reproducibility (s_{Rw})**

$u(R_w)$

Including sample preparation!

- The same analyte
- Ideally:
  - The same sample analysed during long time
  - Sample similar to test samples
    - matrix, concentration, homogeneity
  - The same lab
  - The same method
  - Different days (preferably over 1 year)
  - Different persons
  - Different reagent batches
  - …

$u(R_w)$

$$u(R_w) = s_{Rw}$$

Ideally: separately for different matrices and different concentration levels!

The control sample analysis has to cover the whole analytical process

Repeatability	<	Within-lab reproducibility	<	Combined uncertainty
s_r	<	s_{Rw}	<	u_c

u(bias)

- The *possible* **bias** of lab's results from the best estimate of true value is taken into account

Including sample preparation!

- **Reference value is needed!**
- Reference value and *u*(*bias*) can be found:
  - From the analysis of the same samples with a reference method
  - From the analysis of certified reference materials (CRMs)
  - From interlaboratory comparison measurements
  - From spiking experiments

Ideally: several reference materials, several PTs because the bias will in most cases vary with matrix and concentration range

Replicate measurements!

u(bias)

$$u(bias) = \sqrt{RMS_{\mathrm{bias}}{}^2 + u(Cref)^2}$$

This component accounts for the **average possible bias** of the laboratory results from the C_{ref}

This component accounts for the **average uncertainty** of the reference values C_{ref}

- Bias can actually be zero:
  - We speak about ***possible*** bias
  - Nordtest method can lead to overestimating uncertainty

u(bias)

- The averaging is done using the **root mean square:**

$$bias_i = Clab_i - Cref_i \qquad RMS_{bias} = \sqrt{\frac{\sum (bias_i)^2}{n}}$$

$$u(Cref) = \sqrt{\frac{\sum u(Cref_i)^2}{n}}$$

In the case of ILCs:

$$u(Cref_i) = \frac{s_i}{\sqrt{n_i}}$$

- $bias_i$: i-th bias
- $Clab_i$: Lab's value when deteriming i-th bias
- $Cref_i$: reference value when deteriming i-th bias
- n: number of reference values used
- n_i: number of ILC participants in i-th ILC
- s_i: consensus standard deviation in i-th ILC

Every $bias_i$ is found from replicate measurements!

u(bias): only one CRM

- If only one single CRM is used:

$$u(bias) = \sqrt{bias^2 + s_{\mathrm{bias}}^2/n + u(Cref)^2}$$

- We have just *bias*, not $\mathrm{RMS}_{\mathrm{bias}}$
  - Because there is only one bias determined
- Only one CRM should be used only for the first uncertainty estimate
  - Afterwards more bias estimates should be used

Uncertainty due to possible bias

Evaluation of uncertainty due to bias, ideally:

- **Separately for every analyte**
- **Separately for different sample matrices**
- **Separately for different concentration levels**

If low-quality reference values are used overestimated uncertainties can be obtained

Roadmap:

Possible bias

$u(Cref_i)$ from certificates

$$u(Cref_i) = \frac{s_i}{\sqrt{n_i}}$$

$$u(Cref) = \sqrt{\frac{\sum u(Cref_i)^2}{n}}$$

$$bias_i = Clab_i - Cref_i$$

$$RMS_{bias} = \sqrt{\frac{\sum (bias_i)^2}{n}}$$

$$u(bias) = \sqrt{RMS_{\text{bias}}{}^2 + u(Cref)^2}$$

Uncertainty due to random effects

$$u(R_{\text{w}}) = s_{\text{RW}}$$

Combined standard uncertainty

$$u_{\text{c}} = \sqrt{u(R_{\text{w}})^2 + u(bias)^2}$$

Example:
measurement uncertainty estimation of iron content in seawater

We will do in MS Excel

Data from:

Worsfold PJ, Achterberg EP, Birchill AJ, Clough R, Leito I, Lohan MC, Milne A and Ussher SJ Estimating Uncertainties in Oceanographic Trace Element Measurements. *Front. Mar. Sci*. 2019, 5, 515.
https://doi.org/10.3389/fmars.2018.00515

Thank you for your attention!

Do you wish to learn more?

- Feel free to **contact me**
  - But I am slow with e-mails

- Web course **Estimation of measurement uncertainty in chemical analysis** (1 ECTS)
  - https://sisu.ut.ee/measurement/
  - Mar-May 2025, registration link will be there in Jan 2025

- Course **Metrology in Chemistry** (6 ECTS)
  - Will be lectured at UT in hybrid mode Feb-May 2025
  - It is possible to organise that you can participate online
  - Uncertainty, validation, traceability, CRMs, ILCs, Quality control