The main question of uncertainty evaluation in an analytical lab:

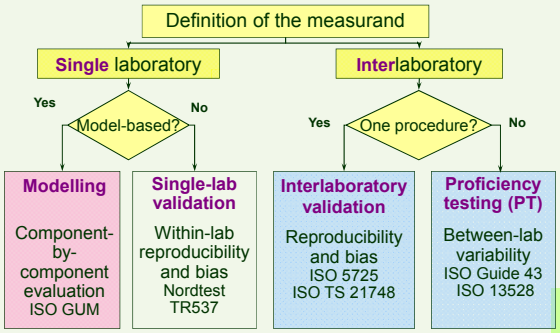
The uncertainty sources are more or less known

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 approaches



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

Approach based on validation and Quality Control Data

aka "the Nordtest approach"

Nordtest Technical Report 537, ed 3.1 (2012)
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 possible bias

Long-term!

Single lab validation approach: in practice (1)

- 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 and the possible procedure bias

This component accounts for the long-term systematic effects

- This and subsequent equations work with absolute and relative values

Nordtest Technical Report 537, ed 3.1 (2012)
http://www.nordtest.info/

Absolute vs relative uncertainties: Rules of Thumb

- **In general: use whichever is more constant**
- **Some rules of thumb:**
  - **At low concentrations (near detection limit, trace level) use absolute uncertainties**
    - Uncertainty is not much dependent on analyte level
  - **At medium and higher concentrations use relative uncertainties**
    - Uncertainty is roughly proportional to analyte level

Single lab validation approach: in practice

Steps of the process:

1*. Specify measurand
2. Quantify R_w component ***u*(*R*w)**
3. Quantify bias component ***u*(*bias*)**
4*. Convert components to standard uncertainties ***u*(*x*)**
5*. Calculate combined standard uncertainty u_c
6*. Calculate expanded uncertainty ***U***

*** Note – general step – the same for modeling (i.e. ISO GUM)**

$u(R_w)$

- $u(R_w)$ is the uncertainty component that takes into account long-term variation of results within lab, that means: within-lab reproducibility (s_{Rw})
- Ideally:
  - The same sample
    - Sample similar to test samples – matrix, concentration, homogeneity
  - The same lab
  - The same procedure
  - Different days (preferably over 1 year)
  - Different persons
  - Different reagent batches
  - …

Including sample preparation

Repeatability < Within-lab reproducibility < Combined uncertainty

s_r < s_{Rw} < u_c

$u(R_w)$

$u(R_w) = s_{Rw}$

Ideally: separately for different matrices and different concentration levels!

The control sample analysis has to cover the whole analytical process

$u(bias)$

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

Including sample preparation

- $u(bias)$ can be found:
  - From analysis of the same samples with a reference procedure
  - From analysis of certified reference materials (CRMs)
  - From interlaboratory comparison me
  - From spiking experiments

Replicate measurements

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

$u(bias)$

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

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

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

u(bias)

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

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

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

- Each $bias_i$ is obtained as an **average of replicate measurements**
  - Only this way is it possible to reduce the random effects

u(bias): only one CRM

- If only one single CRM is used:

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

Uncertainty due to possible bias

Evaluation of uncertainty due to bias, ideally:

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

This approach is rather demanding in terms of availability of sample data

Single-lab validation approach in practice:

Determination of acrylamide in snacks by LC-MS

- Concentration level 998 µg/kg
- Laboratory has analysed two certified reference materials (CRMs) with similar matrixes
  - Potato chips and crisp bread
  - The crisp bread CRM is also used as a control sample

Certified reference material (CRM)

- The **crisp bread** CRM has the following acrylamide content:

$C_{acrylamide}$ = (1179 ± 68) µg/kg (k = 2, norm.)

- The **potato chips** CRM has the following acrylamide content:

$C_{acrylamide}$ = (860 ± 42) µg/kg (k = 2, norm.)

Measurements with the CRMs

Crisp bread

Days	C (mg/l)
5.01.2008	1172
6.03.2008	1186
3.04.2008	1153
8.01.2009	1151
18.03.2009	1181
3.04.2009	1147
11.04.2009	1097
16.04.2009	1102
25.04.2009	1162
3.08.2009	1138
28.08.2009	1122
27.11.2009	1191

Mean:	1150 µg/kg
Std Dev.	31 µg/kg

Potato chips

Days	C (mg/l)
3.04.2008	845
3.04.2008	832
3.04.2008	802
27.04.2008	829
27.04.2008	851
27.04.2008	834

Mean:	832 µg/kg
Std Dev.	17 µg/kg

Roadmap:

Possible bias $u(Cref_i)$ from certificates

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

$$bias_i = Clab_i - Cref_i$$

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

Uncertainty due to random effects

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

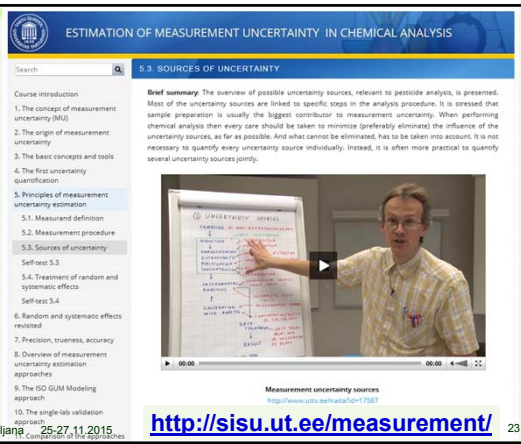
Combined standard uncertainty

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

Finding $u(R_w)$

Finding u(bias)

Result:



http://sisu.ut.ee/measurement/

Thank you for your participation!

- The materials are available from:
  http://tera.chem.ut.ee/~ivo/Temp/QA_Hg_Ljubljana_2015/
- More explanations and examples:
  http://sisu.ut.ee/measurement/
- You are always welcome to contact me:
  ivo.leito@ut.ee

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