Uncertainty estmation approach based on validation and Quality Control Data “the Nordtest approach"

Ivo Leito
University of Tartu
Institute of Chemistry

2013

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**

at „long term“ level!

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 random effects

Uncertainty of the estimate of the laboratory and the method bias

This component accounts for the systematic effects

This and subsequent equations work with absolute and relative values

Absolute vs relative uncertainties: 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
- **In general: whichever is more constant**

**Appendix E.4 from Quantifying Uncertainty in Analytical Measurement, EURACHEM/CITAC Guide, Second Edition (2000)
Available from : http://www.eurachem.org/**

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***

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
  - …

Include 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

7

u(bias)

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

Include sample preparation!

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

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

8

u(bias)

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

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}

9

u(bias)

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

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

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

- *n*: the number of bias estimates used
  - If *n* is too small then the bias component will include a large share of random effects and may be overestimated

10

u(bias): only one CRM

- If only one single CRM is used:

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

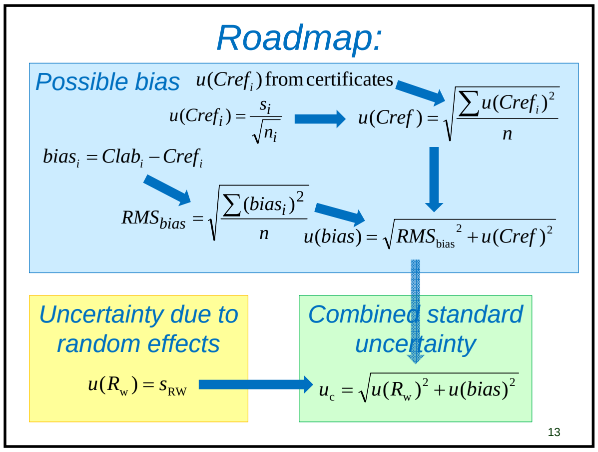
11

Uncertainty due to possible bias

Evaluation of uncertainty due to bias, ideally:

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

12


Roadmap:
Possible bias
$u(Cref_i)$ from certificates
$u(Cref_i) = \frac{s_i}{\sqrt{n_i}}$
$u(Cref) = \sqrt{\frac{\sum u(Cref_i)^2}{n}}$
$bias_i = Clab_i - Cref_i$
$RMS_{bias} = \sqrt{\frac{\sum (bias_i)^2}{n}}$
$u(bias) = \sqrt{RMS_{bias}^2 + u(Cref)^2}$
Uncertainty due to random effects
$u(R_w) = s_{RW}$
Combined standard uncertainty
$u_c = \sqrt{u(R_w)^2 + u(bias)^2}$
13