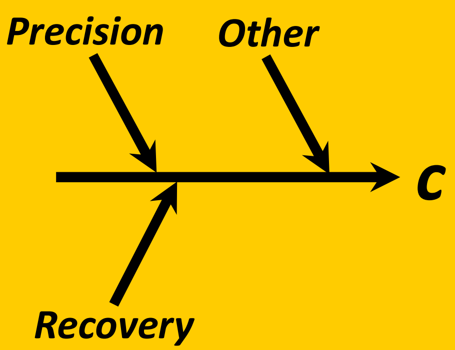
Eurachem approaches to measurement uncertainty evaluation from method validation data



Eurachem
A focus for analytical chemistry in Europe

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Outline

Introductory information
Uncertainty components affecting measurements
Quantification, combination and expansion of the MU*
Final remarks

* - measurement uncertainty

Measurement process

(1) Definition of the problem
(2) Definition of measurement requirements
(analytical scope, target MU* and others)
(3) Method development
(4) Method validation
(culminates with comparing the MU with the target MU)
(5) Analysis of unknown samples supported by test quality control
(6) Decision on tested samples

* - measurement uncertainty

Effects on measurements

Measurements are affected by:
- Within-day random effect (quantified by the repeatability standard deviation, s_r)
- Between days random effects (quantified by the between-days standard deviation, s_b)
- Between days systematic effects

$$s_\mathrm{I} = \sqrt{s_\mathrm{r}^2 + s_\mathrm{b}^2}$$

s_I - intermediate precision standard deviation

Effects on measurements

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- **Within-day random effect** (quantified by the repeatability standard deviation, s_r)
- **Between days random effects** (quantified by the between-days standard deviation, s_b)
- **Between days systematic effects**

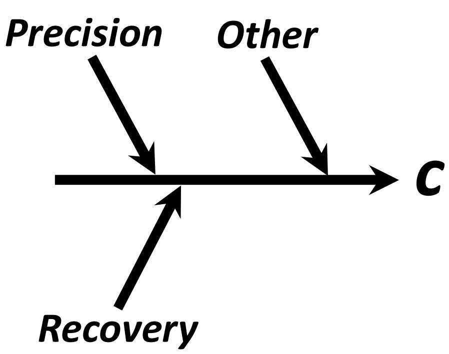
The assessment of systematic effects is always affected by random effects

$$s_I = \sqrt{s_r^2 + s_b^2}$$

s_I **- intermediate precision standard deviation**

Uncertainty components

Evaluation based on in-house method validation:



Precision uncertainty

If a single measurement is performed:

$$u_{\mathrm{P}} = s_{\mathrm{I}}$$

If the result is the mean of *n* measurements performed in different days:

$$u_{\mathrm{P}}(n;\mathrm{dd}) = s_{\mathrm{I}}/\sqrt{n}$$

If the result is the mean of *m* measurements performed in the same day:

$$u_{\mathrm{P}}(m;\mathrm{sd}) = \sqrt{s_{\mathrm{I}}^2 + s_{\mathrm{r}}^2\left(\frac{1-n}{n}\right)}$$

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u_{P} - precision standard uncertainty

Precision uncertainty

For measurements applicable to a wide concentration range, precision models should be defined:

- **Typically, below $2c_{\mathrm{LOQ}}$, s_{I} is approximately constant §**

- **Typically, above $2c_{\mathrm{LOQ}}$, $s'_{\mathrm{I}} = s_{\mathrm{I}}/c$ is approximately constant**

(model is improved if additional intervals above $2c_{\mathrm{LOQ}}$ are considered)

Interval I (c_{LOQ} to $2c_{\mathrm{LOQ}}$): Constant $s_{\mathrm{I}}\langle\mathrm{I}\rangle$
Interval II ($2c_{\mathrm{LOQ}}$ to $10c_{\mathrm{LOQ}}$): Constant $s'_{\mathrm{I}}\langle\mathrm{II}\rangle$
Interval III ($10c_{\mathrm{LOQ}}$ to c_{Max}): Constant $s'_{\mathrm{I}}\langle\mathrm{III}\rangle$

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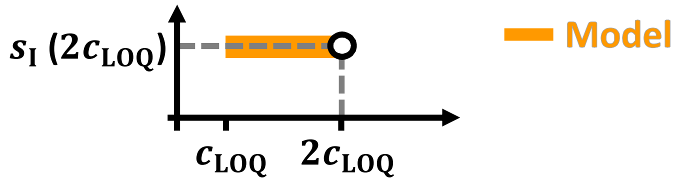
§ - Instead of 2, another multiplying factor can be used.

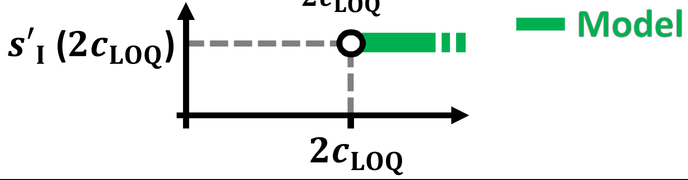
Precision uncertainty – Example A

Quantify s_I at $2c_\mathrm{LOQ}$, $s_\mathrm{I}\,(2c_\mathrm{LOQ})$:

Interval I (c_LOQ to $2c_\mathrm{LOQ}$): $s_\mathrm{I}\langle\mathrm{I}\rangle = s_\mathrm{I}\,(2c_\mathrm{LOQ})$



Interval II ($2c_\mathrm{LOQ}$ to c_Max): $s'_\mathrm{I}\langle\mathrm{II}\rangle = \dfrac{s_\mathrm{I}\,(2c_\mathrm{LOQ})}{2c_\mathrm{LOQ}}$

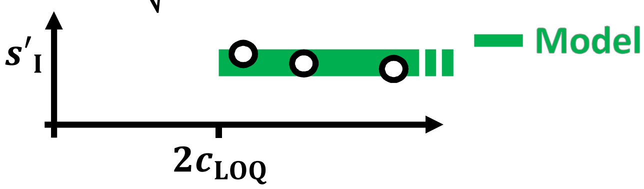


Precision uncertainty – Example B

Intermediate precision from pooling various (*i* or *j*) estimates from N_i or M_i replicates:

Interval I (c_LOQ to $2c_\mathrm{LOQ}$): $s_\mathrm{I}\langle\mathrm{I}\rangle = \sqrt{\sum(N_i-1)s^2_{\mathrm{I}(i)}/\sum(N_i-1)}$

Interval II ($2c_\mathrm{LOQ}$ to c_Max): $s'_\mathrm{I}\langle\mathrm{II}\rangle = \sqrt{\sum(M_i-1)s'^2_{\mathrm{I}(j)}/\sum(M_i-1)}$



Precision uncertainty – Example C

Determination of total As in marine sediments: $c_{\mathrm{LOQ}} = 0.05\ \mathrm{mg\ kg^{-1}}$

Sample	c (mg kg^{-1})	s_{I} (mg kg^{-1})	s'_{I}	n
Interval I: Below $2c_{\mathrm{LOQ}}$				
A	0.0510	0.0052	-	8
B	0.0880	0.0074	-	9
Model: $u_{\mathrm{P}} = \sqrt{\frac{0.0052^2(8-1)+0.0074^2(9-1)}{(8-1)+(9-1)}} = 0.00647\ \mathrm{mg\ kg^{-1}}$				
Interval II: Above $2c_{\mathrm{LOQ}}$				
C	0.120	-	5.3%	10
D	0.452	-	4.9%	11
Model: $u'_{\mathrm{P}} = \sqrt{\frac{5.3\%^2(10-1)+4.9^2(11-1)}{(10-1)+(11-1)}} = 5.09\%$				

Recovery uncertainty

Uncertainty for the management of systematic effects.

- **requires the analysis of samples with known concentration**
- **involves deciding if observed relevant systematic effects should be corrected on results:**
  - **Correct results for relevant recovery if mandatory or allowed**
  - **Do not correct results if correction is not allowed**

Recovery uncertainty

Mean recovery uncertainty

Standard uncertainty, $u_{\bar{\bar{R}}}$, of the overall mean recovery, $\bar{\bar{R}}$, estimated from N mean recoveries, $\bar{R}_i$, determined from the analysis of N reference material in n_i different days:

$$u_{\bar{\bar{R}}} = \sqrt{\sum_{i=1}^{N} \left(\frac{\bar{c}_i}{C_i}\right)^2 \left[\left(\frac{s_{\mathrm{I}}(c_i)}{\bar{c}_i\sqrt{n_i}}\right)^2 + \left(\frac{u(C_i)}{C_i}\right)^2\right] \Big/ N}$$

C_i and $\bar{c}_i$ are the reference and mean of measured values ($\bar{R}_i = \bar{c}_i / C_i$).

Recovery uncertainty

- **Assess if $\bar{\bar{R}}$ is different from 1:**

$$\frac{\left|1 - \bar{\bar{R}}\right|}{u_{\bar{\bar{R}}}} \leq 2$$

yes → **Report original estimate, c**

no → **Report corrected result, $c_c = c / \bar{\bar{R}}$**

Recovery uncertainty – Example C

Determination of total As in marine sediments:
Proficiency test samples:

Sample	C (mg kg^{-1})	$u(C)$ (mg kg^{-1})	$\bar{c}$ (mg kg^{-1})	s_{I} (mg kg^{-1})	n
E	0.1460	0.0234	0.1400	0.0053	7
F	0.2210	0.0236	0.1960	0.0076	12

$$u_{\bar{\bar{R}}} = \sqrt{\left(\frac{0.1400}{0.1460}\right)^2\left[\left(\frac{0.0053}{0.1400\sqrt{7}}\right)^2+\left(\frac{0.0234}{0.1460}\right)^2\right] + \left(\frac{0.1960}{0.2210}\right)^2\left[\left(\frac{0.0076}{0.1960\sqrt{12}}\right)^2+\left(\frac{0.0236}{0.2210}\right)^2\right]} \Big/ 2 = 0.0906$$

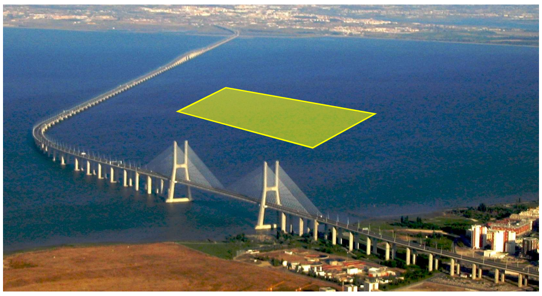
$$\frac{|1-0.923|}{0.0906} = 0.850 \leq 2$$

Additional uncertainty

Relevant components not expressed in u_{P} and $u_{\bar{\bar{R}}}$:

Example:

Sampling uncertainty if an item larger than the laboratory sample is to be characterised.



Eurachem/EUROLAB/CITAC/Nordtest/AMC Guide: Measurement uncertainty arising from sampling: a guide to methods and approaches. Second Edition, Eurachem (2019).

C. Borges, et al., Optimization of river sampling: application to nutrients distribution in Tagus river estuary, Anal. Chem. 91 (2019) 5698-5705

Combination and expansion

Interval I $[c_{\text{LOQ}}, 2c_{\text{LOQ}}]$:

$$U = 2\sqrt{u_{\text{P}}^2\langle\text{I}\rangle + \left(c_{\square} \cdot u'_{\bar{\bar{R}}}\right)^2}$$

Interval II $[2c_{\text{LOQ}}, c_{\text{Max}}]$:

$$U = 2c_{\square}\sqrt{u'^2_{\text{P}}\langle\text{II}\rangle + u'^2_{\bar{\bar{R}}}}$$

where $c_{\square}$ is c or c_c, and U the expanded uncertainty for 95% confidence level.

Combination and expansion – Ex. C

Determination of total As in marine sediments:
Proficiency test samples

	s_{I} (mg kg^{-1})	s'_{I}	$u'_{\bar{\bar{R}}}$
Below $2c_{\text{LOQ}}$			
	0.00647 mg kg^{-1}	-	$0.0906/1$
Model: $U(\text{mg kg}^{-1}) = 2\sqrt{0.00647^2 + (c \cdot 0.0906)^2}$			
Above $2c_{\text{LOQ}}$			
	-	5.09%	$0.0906/1$
Model: $U(\text{mg kg}^{-1}) = 2c\sqrt{(0.0509)^2 + (0.0906)^2} = 0.208c$			

Reported MU

The reported MU does not express performance and the uncertainty of the used references exclusively…

It expresses the way available information was used to quantify, combine and expand the MU

You get ~~what~~ how you see

Final remarks

● Top-down uncertainty evaluations are popular for their simplicity, but frequently some simplifications hide relevant details.

● 24 years after introducing the MU concept in accredited laboratories, this concept is being used seriously in conformity assessments…therefore, we must be more careful in our MU evaluations.

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Thanks for your attention

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