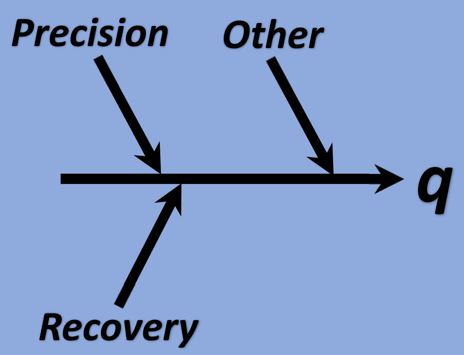
Evaluation of measurement uncertainty based on in-house validation data



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Outline

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

*** - measurement uncertainty**

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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

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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

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

s_I - intermediate precision standard deviation

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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**

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

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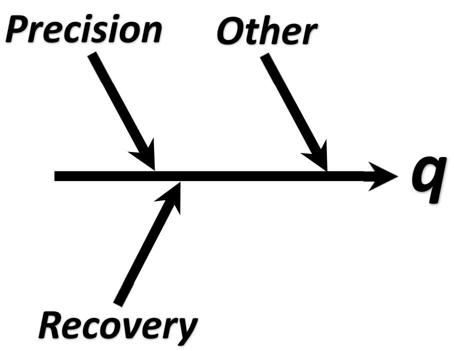
Uncertainty components

Evaluation based on in-house method validation:



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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:

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

u_{P} - precision standard uncertainty

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Precision uncertainty

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

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

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

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

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

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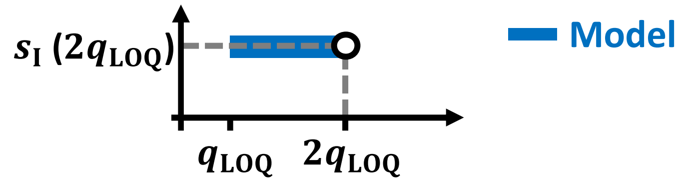
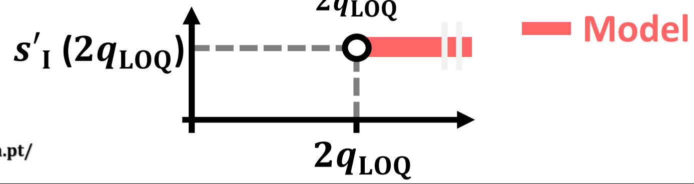
Precision uncertainty – Example A

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

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



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



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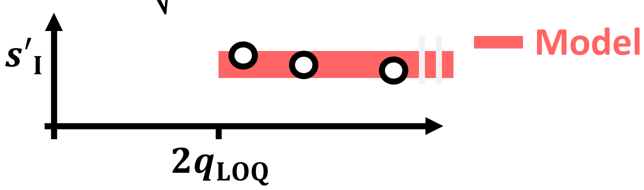
Precision uncertainty – Example B

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

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

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



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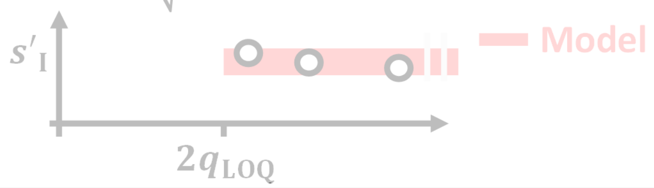
Precision uncertainty – Example B

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

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

Next presentation:
Evaluating the precision component of measurement uncertainty
Bertil Magnusson *[Trollboken, SE]*

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



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Recovery uncertainty

(more details in the following presentation)

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**

Presentation from Day 2:
Handling allowable limits for recovery
Steve Ellison *[LGC, UK]*

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Recovery uncertainty

- **Standard uncertainty, $u_{\bar{R}}$, of the mean recovery, $\bar{R}$**

If $\bar{R}$ is estimated from N single results of the participation in proficiency tests ($\bar{R} = \sum(q_i/Q_i)/N$) where q_i and Q_i are the estimated and reference values:

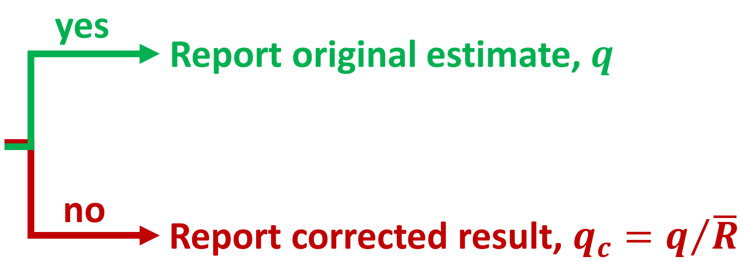
$$u_{\bar{R}} = \sqrt{\sum_{i=1}^{N}\left(\frac{q_i}{Q_i}\right)^2\left[\left(\frac{s_{\mathrm{I}}(q_i)}{q_i}\right)^2 + \left(\frac{u(Q_i)}{Q_i}\right)^2\right]\Big/N}$$

(more scenarios will be discussed in the following presentation)

Recovery uncertainty

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

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



Additional uncertainty

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

Example A:

Sample heterogeneity if samples used to estimate u_{P} and $u_{\bar{R}}$ and more homogenous than "real" samples:

$$u_h = \sqrt{\left(\frac{\bar{A}_{\mathrm{r(h)}}}{1.128}\right)^2 - \left(\frac{\bar{A}_{\mathrm{r}}}{1.128}\right)^2}$$

where $\bar{A}_{\mathrm{r(h)}}$ and $\bar{A}_{\mathrm{r}}$ and the mean range of duplicate results from the analysis of heterogeneous or homogeneous samples under repeatability conditions.

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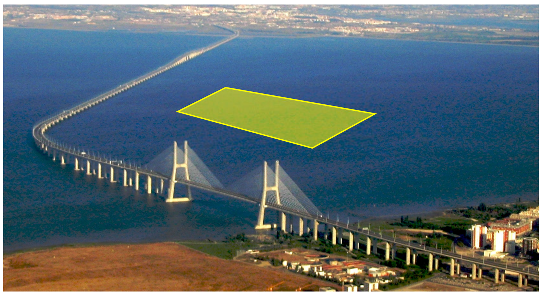
Additional uncertainty

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

Example B:

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

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Combination and expansion

Interval I $[q_{\mathrm{LOQ}}, 2q_{\mathrm{LOQ}}]$:

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

Interval II $[2q_{\mathrm{LOQ}}, q_{\mathrm{Max}}]$:

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

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

Frequent mistakes

- **Inadequate management of precision variation: Relative standard deviation observed above $2q_{\mathrm{LOQ}}$ is not applicable below $2q_{\mathrm{LOQ}}$**

- **Underestimating s_{I} by the standard deviation of results collected on the same and different days**

- **Using more permissible quality control criteria than allowed by the u_{P}**

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

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Final remarks

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

- **22 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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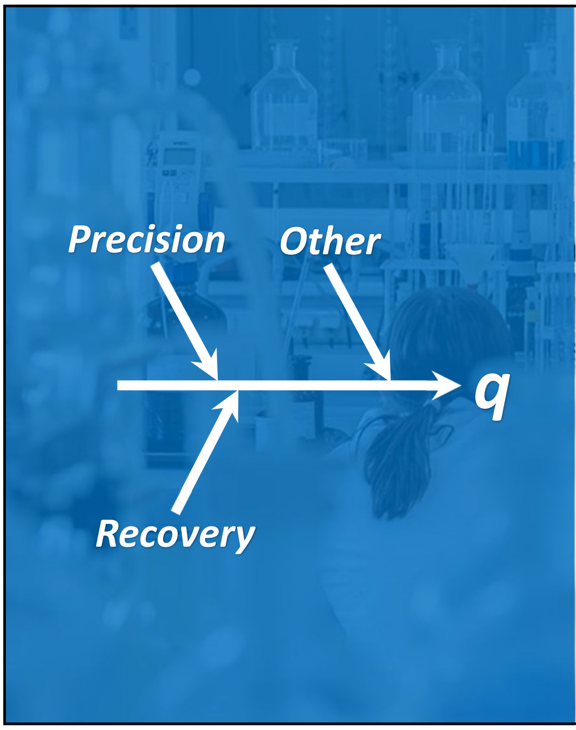

Thanks for your attention

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