Current approaches to the evaluation of measurement uncertainty

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Overview

- Uncertainty estimation process
- 'Bottom-up' vs 'top-down' approach
- Using validation and quality control data in uncertainty estimation
  - requirements for the top-down approach
- Sources of data
- Limitations

Estimating uncertainty – general procedure

Step 1 Be clear about what is being measured — Write down equation used to calculate result.

Step 2 Identify the sources of uncertainty — Parameters appearing in the equation will contribute to the uncertainty. What other factors will influence the result?

Step 3 Quantify uncertainty components — Estimate the size of each uncertainty component (the effect it will have on the result). Convert all estimates to the same form (standard uncertainty, *u*).

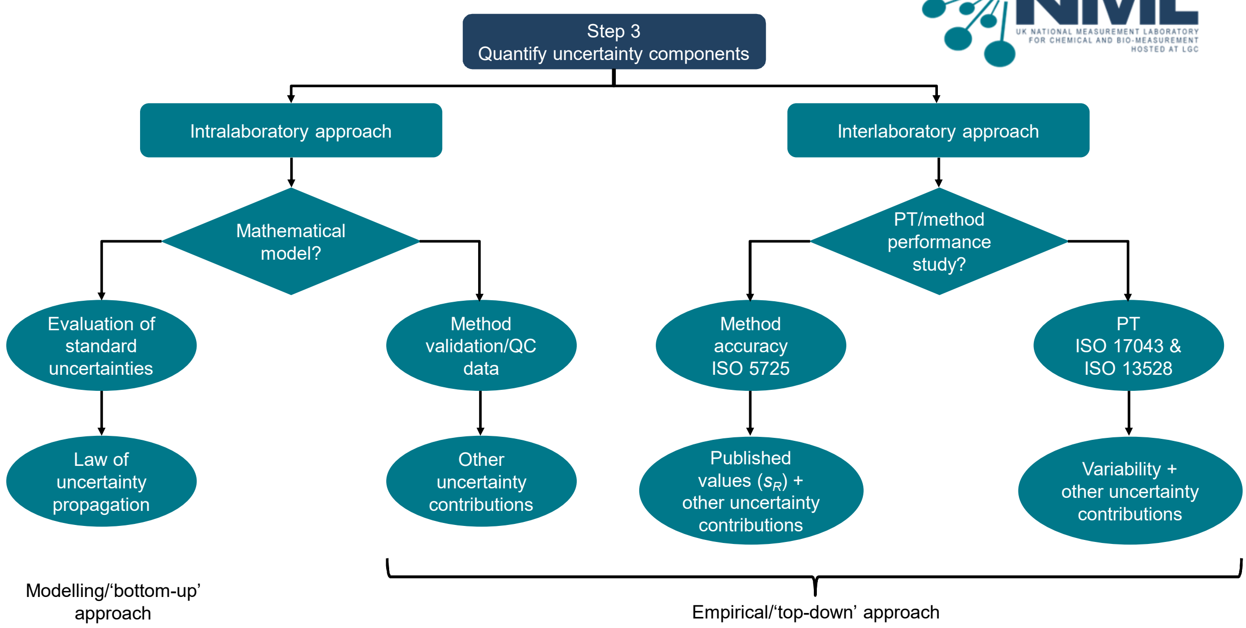
Step 4 Combine the uncertainties — Combine using rules for combination of variances.

$$u_c = \sqrt{u_1^2 + u_2^2 + u_3^2 + \ldots}$$

Step 5 Expand combined uncertainty — Multiply the combined uncertainty by a coverage factor to obtain an expanded uncertainty. $U = k.u_c$

Uncertainty estimation approaches

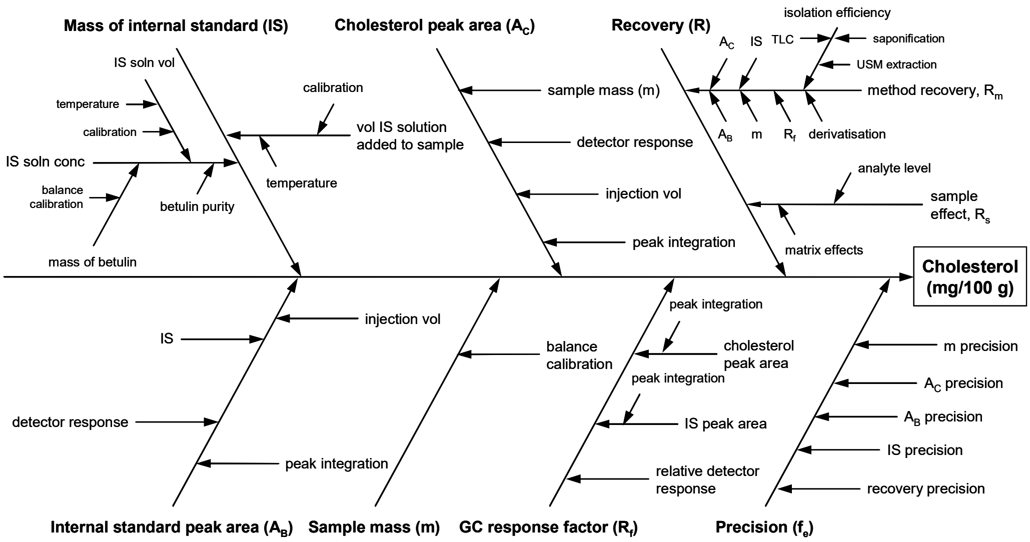
(adapted from Eurolab Technical Report 1/2007, Figure 1)



Modelling approach – ‘bottom-up’

- **Write an equation that completely describes the measurement system**
  - includes all parameters that could influence the measurement result
- **Estimate the uncertainties associated with all parameters in the equation**
  - Type A: statistical evaluation, Type B: any other data (certificates, instrument specifications, etc)
- **Express all uncertainties as standard deviations**
- **Combine using mathematical rules for the combination of variances**
- **Apply a suitable coverage factor**

Can the “bottom-up” approach work for analytical chemistry?



Problems

- **Difficult to write an equation that includes all influence factors**
  - what about sample clean-up conditions, recovery of analyte from matrix, instrument conditions, interferences….
- **Challenging to evaluate individual uncertainty components**
- **Process is too time consuming and unworkable in routine testing laboratories**
  - a 'reasonable estimation' is required

'Top-down' approach

- **Use method performance data**
  - validation data on precision and bias
    - in-house/interlaboratory studies
  - ongoing internal quality control (IQC) data
  - proficiency testing data
- **Capture the effect of a number of sources of uncertainty**
- **Look at the variation in method *outputs* (i.e. results) rather than method *inputs***
- **Cover method scope**
  - matrix, analyte concentration

‘Top-down’ requirements

- **The best available estimate of precision**
  - from validation studies or ongoing QC
- **The best available estimate of bias and its uncertainty**
  - includes method bias and laboratory bias
- **Other significant effects evaluated**
  - by experiment, or from existing data
- **Covering the method scope**
- **Likely scenarios:**
  - for existing data, need to establish what uncertainty components are covered and decide whether any further experiments are required
  - planning a new study: ensure as many uncertainty components as possible are covered

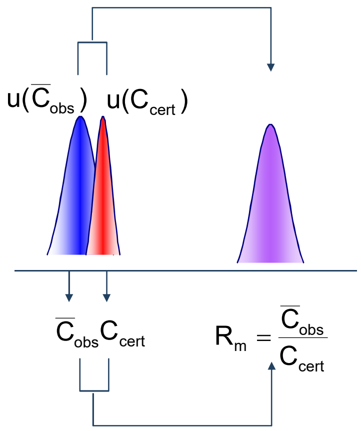
Evaluating precision

- **Aim to cover as many sources of variation as possible**
  - extended time period, different analysts, different calibration standards, environmental conditions
- **A parameter varied representatively during a precision study requires no further evaluation**
- **Types of data**
  - method validation study (intermediate precision)
  - quality control data – repeated analysis of QC materials
  - data from interlaboratory studies (method validation or PT)
- **Need to consider effect of different levels/matrices**

Evaluating bias

- **A reasonable estimate of the bias can be obtained from**
  - validation data (using CRMs or spiked samples)
  - PT data (depending on the nature of the scheme/samples)
- **Is the bias significant?**
  - statistically significant?
  - significant compared to the method precision?
- **Bias and its uncertainty should be considered as part of the uncertainty evaluation process**
- **Need to consider effect of sample matrix on bias/recovery**

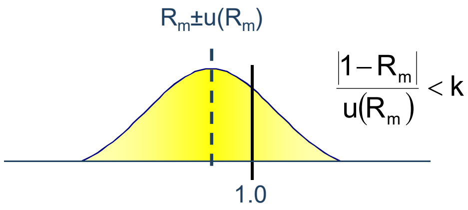
Estimating uncertainty associated with recovery



$$\frac{u(R_m)}{R_m} = \sqrt{\left(\frac{u(\bar{C}_{obs})}{\bar{C}_{obs}}\right)^2 + \left(\frac{u(C_{cert})}{C_{cert}}\right)^2}$$

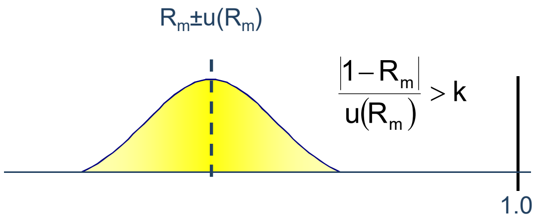
- Estimate of recovery/bias has associated uncertainty
  - uncertainty in reference value $u(C_{cert})$
    - from CRM certificate – convert to standard uncertainty
    - uncertainty in calculated concentration of spiked sample
    - express as a relative value
  - uncertainty in mean of results $u(\bar{C}_{obs})$
    - standard deviation of the mean of results for CRM or spike sample ($s/\sqrt{n}$)
    - express as a relative value

Is there a significant bias?



R_m not significantly different from 1

=> no significant bias



R_m significantly different from 1

=> significant bias

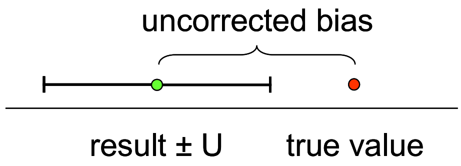
Including bias in uncertainty estimates (1)

- **Insignificant bias – recovery not significantly different from 100%**
  - assume R_m = 1 with an uncertainty, $u(R_m)$
- **Significant bias**
  - develop method to remove/reduce bias
  - correct results for known significant bias (ISO Guide)
    - include $u(R_m)$ in uncertainty estimate for corrected results
  - correction uncommon in chemical analysis

Including bias in uncertainty estimates (2)

Uncorrected bias

- Uncertainty is a range which includes the true value….



- …so significant bias should not be ignored
- Options: report bias and its uncertainty separately OR increase reported uncertainty to take account of the bias

Including bias in uncertainty estimates (3)

- If a separate report of bias or recovery is not appropriate
  - increase reported uncertainty by including a bias uncertainty term
  - bias term combined with precision using "root sum of squares" rule
- Different approaches proposed for estimating bias term
  - root mean square (RMS) of bias estimates
  - mean bias
  - bias divided by coverage factor, k
- Further information in the literature
- However – all have limitations

Limitations of top-down approach

- No information on main sources of uncertainty
- Uncertainty will apply to any future result obtained within scope of method
  – uncertainty estimate needs to address effects of sample matrix/analyte level
- Single estimate may not be possible if MU varies with level/matrix
- Including effect of uncorrected bias
  – different approaches exist

Summary

- The ‘bottom-up’ approach is impractical for many test methods
- The ‘top-down’ approach utilises method performance data
  – requires a reliable estimate of method precision and information on bias
  – available from method validation studies, QC and PT
- ‘Fit for purpose’ for testing laboratories
- …but no information on main sources of uncertainty