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

Step 2
Identify the sources of uncertainty

Step 3
Quantify uncertainty components

Step 4
Combine the uncertainties

Step 5
Expand combined uncertainty

Write down equation used to calculate result.

Parameters appearing in the equation will contribute to the uncertainty. What other factors will influence the result?

Estimate the size of each uncertainty component (the effect it will have on the result). Convert all estimates to the same form (standard uncertainty, $u$).

Combine using rules for combination of variances.

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

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)

Step 3
Quantify uncertainty components

Intralaboratory approach

Mathematical model?

Evaluation of standard uncertainties

Law of uncertainty propagation

Interlaboratory approach

PT/method performance study?

Method accuracy ISO 5725

Published values ($a_p$) + other uncertainty contributions

Variability + other uncertainty contributions

Published values ($a_p$) + other uncertainty contributions

Empirical/'top-down' approach

Modelling/'bottom-up' approach
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

\[
\frac{u(R_m)}{R_m} = \sqrt{\left(\frac{u(C_{\text{obs}})}{C_{\text{obs}}}\right)^2 + \left(\frac{u(C_{\text{cert}})}{C_{\text{cert}}}\right)^2}
\]

- Estimate of recovery/bias has associated uncertainty
  - uncertainty in reference value \( u(C_{\text{cert}}) \)
    - from CRM certificate – convert to standard uncertainty
    - uncertainty in calculated concentration of spiked sample
    - express as a relative value
  - uncertainty in mean of results \( u(C_{\text{obs}}) \)
    - 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?

\[ R_m \pm u(R_m) \]

\[ \frac{|1 - R_m|}{u(R_m)} < k \]

\( R_m \) not significantly different from 1

=> no significant bias

\[ R_m \pm u(R_m) \]

\[ \frac{|1 - R_m|}{u(R_m)} > k \]

\( R_m \) 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….

\[ \text{uncorrected bias} \]

\[ \text{result } \pm U \quad \text{true value} \]

• …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