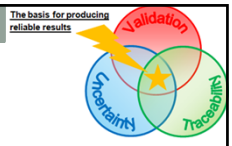


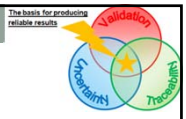
VALIDATION
TRACEABILITY
MEASUREMENT UNCERTAINTY
CHALLENGES FOR THE 21ST CENTURY'S ANALYSTS

Workshop group 1.4:

Combination of MV and MU studies

Convener: Steve Ellison

Rapporteur: (…as convener)



Workshop group 1.4 – participants:

- Ertas, Hasan (TR)
- Golze, Manfred (D)
- Gundrum, Christina (D)
- Hill, Peter (D)
- Karakaya, Mevlana (D)
- Patriarca, Marina (I)
- Sander, Norman (D)
- Todoric, Ijiljana (SLO)

WG 1.4 questions

a. Do you normally combine method validation with estimation of measurement uncertainty in your laboratory?
b. Which information can be taken from a method validation study to the estimation of measurement uncertainty?
c. How do you deal with the reproducibility of a method - and how do you relate that to Measurement Uncertainty?
d. Do you plan your ruggedness testing in the method validation to also give contributions to your measurement uncertainty estimation?
e. Do you participate in interlaboratory comparisons (collaborative trials) as a part of your method validation studies – and does the give information for your measurement uncertainty estimation?
f. Do you re-evaluate results from your method validation after a period, where you have established a better basis for the actual measurement uncertainty on your results from the method?
g. How do you relate Measurement Uncertainty to the performance criteria for a method?
h. Is the fitness of the magnitude of the measurement uncertainty, within the analytical range, the only requirement actually needed to be tested?

a) Do you normally combine method validation with estimation of measurement uncertainty in your laboratory?

- Sometimes ...always for accredited test methods
  - Validation data is used
  - MP:
    - Standard methods have prior data – use reproducibility for MU
    - In-house methods – use intra-lab (”intermediate precision”) + RM data
  - Some labs list uncertainty sources before method validation
    - This can affect validation plans
    - May direct work on (eg) sample stability more than the end measurement

b) Which information can be taken from a method validation study to the estimation of measurement uncertainty?

- Accuracy* and precision
  - repeatability and reproducibility
  - *Does not always mean 'recovery' – Recovery is always important
  - Also use PT data to inform Bias
  - Calibration curve uncertainties sometimes important
  - LOD is not used in MU determination
    - because ....
      - the uncertainty 'defines' the LOD...
      - below the LOD it is not useful to talk about MU

b) …cont.

- Ruggedness
  - Not usually done for standard procedures
  - Sometimes needed to check operations that are incompletely specified
  - (Not all standards give ranges – few old standards give metrological characteriscs of instruments/equipment used)
  - Ruggedness checks give limited information on effect sizes; can help distinguish non-linear response etc.

c) How do you deal with the reproducibility of a method - and how do you relate that to Measurement Uncertainty?

- Published reproducibility
  - Some use ISO 21748 (u is approximately equal to s_R)
  - but **very** different values for s_R cause trouble
    - conservative reporting.
  - Some would only report their own uncertainty estimate

- Using reproducibility SD
  - 'added' to allowance for 'possible' bias* (eg from PT or RM)
  - Not clear whether bias is systematic over the long term or a random effect for a comparatively short time

c) …cont.

- Within-lab reproducibility Design:
  - Some labs change staff or instruments intentionally;
    - (Protocols for 1 or 2 staff)
  - others 'allow' random change
  - Some use QC chart data for reproducibility SD

- Also check instrument performance before and after calibration/servicing

d) Do you plan your ruggedness testing in the method validation to also give contri-butions to your measurement uncertainty estimation?

- Considered above [see b) cont..]
- Some labs plan ruggedness based on measurement uncertainty sources; others do not link the two

e) Do you participate in interlaboratory comparisons (collaborative trials) as a part of your method validation studies – and does the give information for your measurement uncertainty estimation?

- Sometimes used
- Some labs also use this for uncertainty estimation

f) Do you re-evaluate results from your method validation after a period, where you have established a better basis for the actual measurement uncertainty on your results from the method?

- Labs have re-validation intervals
  - eg 5 years or less
- Some update uncertainty budgets
- New equipment or personnel will often trigger revalidation and re-evaluation of uncertainty

g) How do you relate Measurement Uncertainty to the performance criteria for a method?

- [Not discussed this time]

h) Is the fitness of the magnitude of the measurement uncertainty, within the analytical range, the only requirement actually needed to be tested?

- NO
  - because..
    - Preparation (of samples) should be considered
    - Homogeneity may be important
    - Sampling is often important
    - Sometimes precision and bias are individually important

Additional subjects discussed

- Bias
- Top-down and bottom-up uncertainty evaluation?
- Reference material uncertainties
- Dealing with large ‘scope’ – many matrices

Bias

- Using bias information still seems controversial
  - Use the whole bias as an uncertainty?
  - Use the uncertainty in the bias?
  - Use both?
- Use of bias depends on whether bias is 'significant' or not.
  - Not always possible to correct – rarely have a sample-specific correction
- Keeping the bias uncertainty
  - ... is not always 'sensible'
  - ... and may need clarification
- May be able to demonstrate that it is 'not sensible' to include uncertainty from every test

.. and what about top-down and bottom-up uncertainty evaluation?

- Which is appropriate when?
- Depends on whether a good model is available
  - The Eurachem Guide starts with what *information* is available

… and reference material uncertainties?

- CRMs to check trueness may have large uncertainties
  - … and that stays with you
  - (see bias discussion above!)
- Calibration materials
  - Calculating uncertainty for matrix-matched calibration materials prepared by spiking etc.
    - Uncertainty may be non-negligible
    - May change regression statistics
      - (error-in-variable regression?)
      - - but see also Appendix E

… and dealing with large 'scope' – many matrices

- Validation data may not be directly relevant to a particular test sample
- Typical validation uses a small number of 'representative' matrices
- Tends to result in 'conservative' uncertainty reporting
  - report the biggest uncertainty
  - Sometimes use 'pooled' sd.
- (Not all users use uncertainty!)