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Workshop
Method Validation in Analytical Sciences
Current practices and future challenges

Gent, 9-10 May 2016

Report from WG 1 Day2

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Determination of trueness / bias

- Moderator:
  - Bertil Magnusson, SP Sweden
- 30 participants

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Different approaches to determine bias?

- CRMs
- Spiking
- Comparison with another lab or reference method
- ILC, PT particularly:

  over time, typical samples

  Note - common bias of all labs

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of sample types and # of measurements

- MV Guide – 10 measurements at least
- Common - 3 levels: 6 replicates, 8 replicates, 6-10 replicates
  - # of measurements / matrix
- Stability of samples may be an issue
- Risk analysis - # of CRMs & # of measurements
- CI and degree of freedoms
- Spiking of real test samples
- Levels: limit in legislation
- What is more beneficial: # of matrices or # of levels

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Spiking

- Corrects only for proportional effects
- Recovery tests: influence of chemical form of a spike vs. Incured form of an analyte in sample, eg pesticide residues
  - absence of assigned value

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Matrices – number of samples

- Look at the scope – cover the extremes
  - Several guidance
  - Soil analysis in the UK – 3 matrices (clay, sand)
  - Food – extremes hig protein, high fat…
  - Pharma: limited # of matrices
  - Laboratories with flexible scope of accreditation
  - Multivariate methods – representative matrix
  - Validation only for the most difficult matrix – big bias
- Some methods can easily cope with different matrices others cannot
  - Destructive method vs. Extraction
    Statistical approach – Pareto, DoE, factorial design

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How to assess significance of bias

- t-test of significance
  - One or two sided?
  - Difference from 0 – two sided t-test
  - Taking into account standard uncertainty of reference value
- Criterion bias smaller than 10 %
- Significance – is bias too big
  - Comparing bias with requirements

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Significant bias – what to do

- Look at the method again, optimization
  - Influence of the analyst?
  - Matrix calibration
- Is it OK with client's requirements?
- Correction factor
  - How to make correction: factor or difference, eg extraction efficiency
  - Influence of a matrix
- Will decreaing of a bias influence/increase MU?
  - Is increased MU OK for a customer?
- Statistical/metrological significance of a bias

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Challenges experienced in different areas?

- Clinical chemistry – different ways to assess bias: real test samples & reference method
- Demonstrate equivalence – same size of bias
- Development in analytical instrumentation
- Guidance for correction is missing

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Guidance documents you can recommend

- Eurachem MU Guide – pesticides in bread
- NMKL – 2 procedures: validation, CRMs
- Eurolab
- ISO Guide 33 – usage of CRMs
- Nordtest TR 537 – guidance on how to include bias in uncertainty.
- IUPAC recovery document
- ABC paper about bias by Ellison & Magnusson