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METHOD VALIDATION IN ANALYTICAL SCIENCE
Current Practices & Future Challenges
WORKSHOP - 9&10 MAY 2016 - GENT - BELGIUM

WG2 – Planning of validation studies

Convenor:
Vicki Barwick

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Outcome of WG 1.1-2 (LS)

- WG participants
- Belgium 1111111111111
- Steel analysis
- Official Medical control auth.
- Water analysis 11
- Sweden 111
- Medical lab. 11
- Czech 11
- Univesity (Pham.) 1
- University (Research) 111
- Austria
- University X-Ray
- Agricultural related tests 111 (incl. research, animal prod.)
- Ireland
- Italy
- Food safety (contamintants etc.)

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Outcome of WG 1.1-2 (LS)

- Iran
- Consultant
- UK
- Setting specifications on methods for UK Ph.
- Nuclear power supply
- Textile
- Fruits and vegetables
- Poland
- NAB (expec. water labs., fuel)
- NAB
- Food & Feed (trace elements)
- PU field
- Greece
- University (food & envrironmentatl)

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What are the different planning approaches applied in different fields?

- Easy to find info on 'raw ingredients' of a validation but difficult to plan the detail – especially in labs that carry out a wide range of analysis on different materials using different techniques
- In-house protocol based on external guidance
- Generally studying one parameter at a time rather than combined experiments
  - Interested in multi-performance parameter approach described by Steve!

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Outcome of WG 1.1-2 (LS)

- What are the different planning approaches applied in different fields?
- Follow specific regulatations (Food & feed)
  - nat./EU/International regulations (necessary to be aware)
  - depending of the sample types (matrices)
  - requires a case by case planning of Val. studies
- Different regulations for eg. Cd & Cu
  - requires different approaches in val.. studies (different limit values etc.)
- Too many demands on how to validate a method
  - different (not-hamronized) approaches from different authorities
  - more active approach from EU / ISO or other authorities in harmonizing requirements

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What are the protocols available

- Are there any specified protocols/formats for specific fields?
  - Pharmaceuticals – ICH guidelines – but still some decisions to be made by the lab on no. replicates
  - Microbiology – in-house SOP based on external guidelines
  - General – there are guidelines but few protocols
  - Don't forget books with good examples!
  - There are 'local' regulations in certain sectors which give more details
  - A limited number of sectors/regions have very detailed protocols (e.g. UK MCERTS)

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How do you decide about the extent of validation needed?

- Strategies for optimising/combining experiments and/or information
  - Screening vs confirmations – less validation for screening (selectivity/specificity/LOD)
    - Confirmation – full validation
  - Factors to consider:
    - Time (particularly for ad-hoc methods)
    - Customer requirements
    - Equipment/staff availability
    - Scope of method – range of sample types
    - Verification vs validation
    - Requirements of relevant regulations in terms of extent of validation and performance targets

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How do you decide about the extent of validation needed?

- Deciding number of replicates
  - Look at external guidance for help
  - Follow internal SOPs
    - Based on previous experience
  - Ensure that required working range is covered
  - Ensure measurements are made on different days
  - Replication should cover whole method not just end measurement (independent reps)

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Outcome of WG 1.1-2 (LS)

- How do you decide about the extent of validation needed?
  - Strategies for optimising/combining experiments and/or information
- If you follow the exact procedure in a Standard method only verification against ”known” results is needed!
  - what to compare with
  - use of reference materials
  -
- Use data from ILCs (PTs)
  - for validation and/or verification
- Spiking experiments for verification of a standard method ”better than doing nothing”
  -
- Does the laboratory always have all the needed ”tools” for doing validation/verificatin
  - checklist on available tool as part of planning
  - The question is whehter it is good enough?

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Outcome of WG 1.1-2 (LS)

- Pharm: Meth. delivered by producer + some methods to be developed by laboratory
  Interlaboratory studies on ruggedness – securing safe transfer of method to other labs.
- For some fields reference methods (or techniques) exists (related to regulation)
  - comparison mandatory
  - good performance in a PT is not always enough
- Validation of basic chemical method – and a quick (instrumental) method
  - comparisons

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What are the challenges experienced in different areas?

- Varied types of analysis in a lab so not possible to have a single protocol
- Lack of reference materials
- General availability of suitable standards or other materials for evaluating different parameters
- Protocols/guidance assume that labs have access to suitable materials
- Assigning values to in-house standards where no/limited availability of external standards

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What are the challenges experienced in different areas?

- Not always possible to meet initial performance targets so may need further development – takes time!
- Limited information to enable setting performance targets (particularly when working with 'novel' compounds
- Inconsistent definitions/interpretation between different guidelines (e.g. LOD)
- Audits – differing interpretations of requirements

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When is a verification sufficient – and when is a (partial) (re)validation required?

- When can adaption of a method so that it can be performed in a particular laboratory be handled by verification…
- …or when is it to be considered as a modification which requires validation?
- Change in matrix/analyte/level
- If a change is made, carry out an impact assessment to determine the extent of revalidation required
- Periodic review of methods (defined interval) to decide whether method is still fit for purpose
  - Any significant changes? Re-validation required?
- Review of QC/PT
- Quality incidents (e.g. complaints)

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- Verification – fewer parameters/less replication
  - Standard methods (externally validated)
  - Minor changes to method

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Outcome of WG 1.1-2 (LS)

- When is a verification sufficient – and when is a (partial) (re)validation required?
  - When can adaption of a method so that it can be performed in a particular laboratory be handled by verification…
  - …or when is it to be considered as a modification which requires validation?
- Also influenced by regulatory requirements in some cases
- Different approaches for eg. clean water and waste water (approach build up through accreditation – no formal requirements!)
- Clinical field:
  - requirements seems to increase along with new techniques coming up (e.g. in microbiology)
- Scope description of method is important
  - influences what is needed in terms of validation and (not least) verification
  - e.g. in relation to potential interference problems

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What information should a good validation protocol contain?

- Method scope & outline of method
- Purpose of study (validation/verification)
- Explanation strategy (particularly any limitations)
- Samples (no of samples), matrices, levels etc, RMs/standards
- Performance parameters & performance criteria
  - Level of replication
- Sequence of analysis
- Calculations of parameters and statistical tests
- References to any key documents
- Documentation of validation – sufficient data available for someone else to verify claims

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Outcome of WG 1.1-2 (LS)

- What information should a good validation protocol contain?
- The relevant val. characteristics
- Scope of the method
  - based on demand from clients
  - information about purpose of test + background and composition of samples
  - sometimes given in regulation
- Formal requirments (regulations)
- Levels, replicates, materials, time-frame

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Outcome of WG 1.1-2 (LS)

- Challenges in finding appropriate reference materials
- Verification vs. validation
  - be aware of not using the term ”verified” methods (not having the same value among clients)

- Recent developments in knowledge about e.g. contaminants etc. cna call for re-validation
  - follow development of what is really ”fit for the purpose”