Extent of Method Validation

How much validation is enough?

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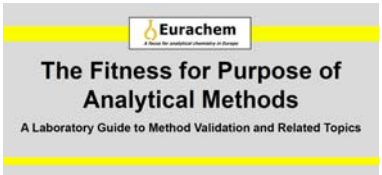
EURACHEM Method Validation Working Group

- This presentation is based on the work done in the EURACHEM MV-WG
- The WG has developed and frequently revised the guide



- As part of the ongoing work of the WG a new supplement is in preparation:

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EXTENT OF METHOD VALIDATION
Efforts to be spent by a laboratory to ensure fitness for purpose of a method

DRAFT 1

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Content of this presentation

- Introduction
- From method verification to stringent method validation
- Validity of a method – fitness for a given purpose
- Extent of method validation and risk management
- Basic steps of the risk assessment
- Conclusions

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Introduction

- Extent of method validation: what and how much?
- What typical performance characteristics? Selectivity, LOD, LOQ,…
- How many experiments for each performance characteristic? 3-6-10?
- Can be based on statistical power calculations
- BUT other issues e.g. limited resources: financial, time, personnel…

➡ **RISK BASED APPROACH**

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From method verification to stringent method validation

Situations in the laboratory:

- Publication of a standard method: stringent method validation required
- Development of an in-house method: single case or routine
- Modification of a standard method
  - To change/expand the scope
  - To change one or more steps in the method
  - To use an alternative equipment
- Method verification: prove that an already validated method works in the lab
- Method transfer

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What is VALID?

*Analytical result must be **sufficiently reliable** that any **decision** based on it can be taken **with confidence**. Thus the method performance must be **validated** and the **uncertainty on the result**, at a given **level of confidence**, estimated.* (Fitness for purpose Guide)

- What is sufficiently reliable?
- What is a given level of confidence for the uncertainty on the results generated by a method?
- Are some methods more valid than others?
- Is a method valid for analyzing meat also valid for analyzing fish?

➡ **METHOD PURPOSE**

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Fitness for purpose

Client / customer

Purpose: Needs to make a decision based on certain knowledge about a sample

Fit for the purpose = Valid

Laboratory

Fitness: Needs to make a decision about what method is fit for the purpose

Method development

Method VALIDation

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What is the method purpose?

3 different types of purposes:

- The purpose of applying the method: what kind of analytical tasks must the method be capable of handling?
- The purpose of using the results produced by the method. What kind of decisions are to be taken based on those results?
- The purpose of performing in routine reliably: What kind of prove can be provided that the method performs reliably in the routine application?

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Fitness for the analytical task (1)

- Impact on performance characteristics to be validated: Low levels or high levels? LOD needed or not?
- Which matrices will be delivered: E.g. meat and vegetables, appropriate method scope, representative matrices to be validated?
- Quality of routine samples: Impurities? Interferences?

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Fitness for the analytical task (2)

Validity of method

- Risk with the laboratory validating/verifying the method
- Analytical task needs to be very well understood
- Close communication between laboratory and client

→ **proper risk assessment to determine extent of method validation**

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Fitness for decision making (1)

- Purpose of the results: to clarify a situation
- Consequences of making a wrong decision are significantly different from situation to situation
- E.g. blood results for diagnosis vs indication salt concentration in water
- Validity of method important in all situations…
- …but extent of method validation may depend on the consequences of making a wrong decision based on the results

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Fitness for decision making (2)

Validity of method

- Risk with user of results / decision maker
- Decision(s) to be made on results need to be well understood
- Close communication between laboratory and client

→ **proper risk assessment to determine extent of method validation**

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Fitness to ensure reliable results routinely (1)

- Often method verification needed (laboratories using standard methods)
- Competence of the laboratory? The laboratory should build up sufficient knowledge and experience to become competent in the method applied.
- Monitoring of method over time (QC) may lead to additional validation
- Stringent method validation for methods to become standard methods for routine use in many laboratories

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Fitness to ensure reliable results routinely (2)

Validity of method

- Risk with both laboratory and client
- Method verification until stringent method validation
- Close communication between laboratory and client: e.g. sample quality, frequency, time constraints

proper risk assessment to determine extent of method validation

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Extent of method validation and risk management

Extent of method validation

- Based on recommendations in FfP guide
- Following statistical power calculations

Disclaimer: these are ideas currently under discussion in the EURACHEM MV-WG and therefore cannot be seen as an official position of EURACHEM

But

- Potential mismatch in resources (time, personnel, money,…)

May lead to a **limited method validation/verification**

→ **risk assessment to determine extent of method validation**

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Basic steps of the risk assessment (1)

1. Preparatory steps

1.1 Communication with the client to

- Clarify the 3 purposes of the method (analytical task – decisions – routine)
- Discuss resources available
- Discuss aspects of expected routine samples, frequency, time constraints,…
- Agree on the decision of extent of method validation

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Basic steps of the risk assessment (2)

1.2 Decide on an initial extent of method validation

- Answer the question “what” to validate, which performance characteristics?
- Answer the question “how much” to validate, per performance characteristic
- As recommended in the FfP guide
- Based on statistical power calculations

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Basic steps of the risk assessment (3)

2. Qualitative risk assessment

- List all consequences related to the extent of method validation chosen
- Potential impact on fitness for purpose of the method
- Risks of accepting method not fit for the purpose
- Risks of not accepting method fit for the purpose

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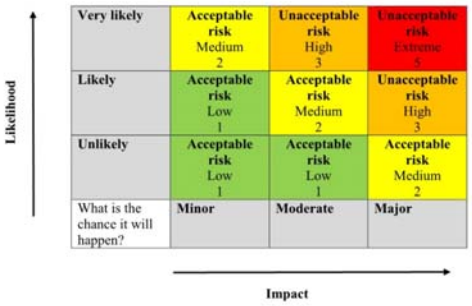
Basic steps of risk assessment (4)

3. Quantitative risk assessment



When

- Outcome shows only acceptable risks: method validation can be approved
- Outcome shows unacceptable risks: discussion with client on resources and purpose of the method – extent to be re-evaluated

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Conclusions

- Fitness for purpose: 3 purposes to be considered
- Analytical task / decisions based on results / routine
- Communication between laboratory and client is important
- Extent of validation needs to be checked in a risk assessment

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Questions or comments?

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Thank you

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