Introduction to method validation

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Overview

- What is method validation?
- Why is method validation necessary?
- When and how do you validate a method?
- Method performance parameters
- How do you assess fitness-for-purpose?

What is validation?

'The **confirmation** by examination and the provision of **objective evidence** that the particular requirements for a **specific intended use** are fulfilled'

- specific intended use = analytical requirement
- objective evidence = experimental data (method performance parameters)
- confirmation (from comparison of requirement with evidence)

[ISO/IEC 17025 definition]

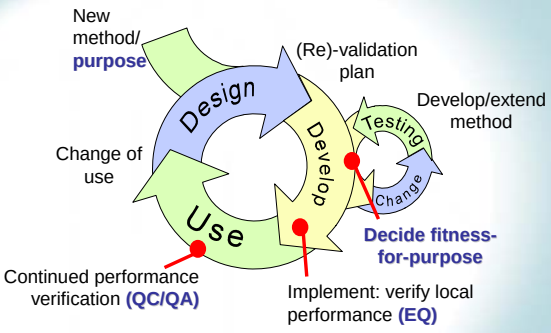
Why is method validation necessary?

- Ethical
  - establish fitness-for-purpose on customer's behalf
  - good science
- Commercial
  - "due care" in product liability
- Regulatory/regulatory
  - legal requirements
  - consistent application of method
  - comparability between analysts / laboratories / countries

When do you validate a method?

- During method development
- Before using any method for samples
  - verify own ability to match published data
  - verify suitability for analytical requirement
- Change of application / working environment / analyst
- Following period of non-use

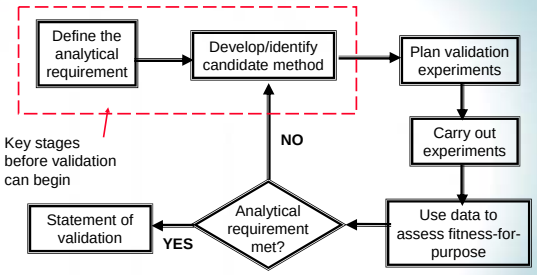
Method development lifecycle



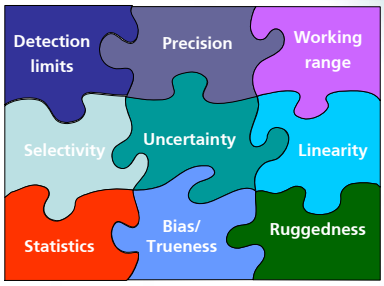
Who validates a method?

- The analyst
  - in-house development and validation of new methods
  - verification of the performance of previously validated methods
- The laboratory
  - method development and validation section
- Sectoral/professional/standardization body
  - validation of methods via interlaboratory study

How do you validate a method?



A validation puzzle

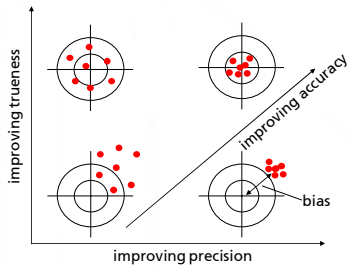


Method performance parameters

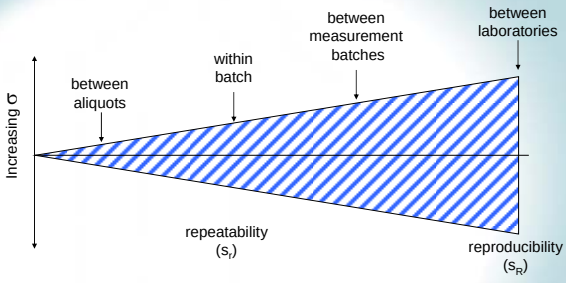
Providing evidence that the method produces results that are fit-for-purpose

- Precision (repeatability, reproducibility)
  - how close are the results of replicate measurements made on the same sample?
- Bias, recovery
  - how close are the results to the 'right' answer
- Working range (LoD, LoQ, Linearity)
- Ruggedness/robustness
  - control necessary for each stage of the procedure
- Selectivity/specificity
  - are there any interferences?

Measures of quality
Precision, bias and accuracy

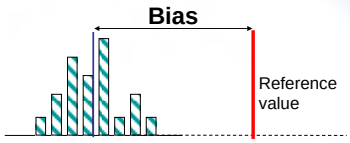


Different precision measures



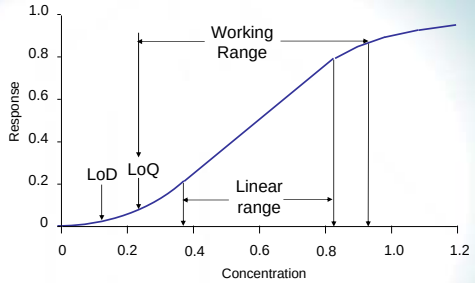
Precision is expressed as a standard deviation or relative standard deviation

Bias



- Replicate analysis of reference material
- Bias = difference between mean value of analytical results and reference value
- Bias is a measure of *Trueness*

Working & linear range



LoD = Limit of Detection

LoQ = Limit of Quantitation

Ruggedness testing

- Key experimental parameters affect the method performance
  - small variations in these parameters cause method performance to change
  - need appropriate control
- Ruggedness testing identifies key parameters
  - make deliberate changes to method parameters
  - observe effect on results
- Control key parameters
  - results in a rugged method

Fitness-for-purpose

- Analyse data from method performance parameters
- Are target values achieved?
  - YES - method is fit-for-purpose
  - NO - more development required
- Method is validated by the declaration of fitness-for-purpose

Summary

- Method validation is required to produce meaningful data
- Both in-house and standard methods require validation/verification
- Validation should be a planned activity
  - parameters required will vary with application
- Validation is not complete without a statement of fitness-for-purpose