Building a validation protocol

Science
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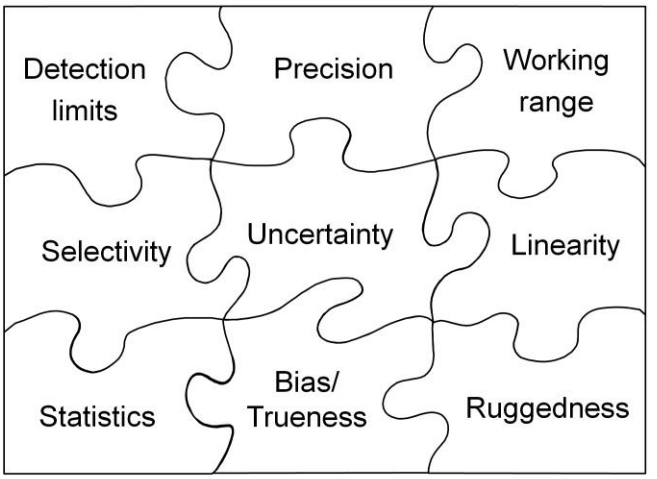
A validation puzzle



Method validation is a process of developing a sufficient picture of a method's performance to demonstrate that it is fit for an intended purpose. The process is based on determination of a range of performance characteristics of the method. Some are quantitative (bias, trueness, precision, detection limits); others qualitative or semiquantitative (ruggedness, selectivity).

Though it is safe to say that a validation is most unlikely to be adequate without some study of overall precision and bias, there is no entirely general order of preference or relevance; different circumstances will place emphasis on different aspects of the process. Most jigsaws yield a recognisable picture without all the pieces; validation is no exception.

The analogy can be extended somewhat; substantial effort will provide a more sharply focused picture than a short study.

It inevitably falls to the analyst to decide, with sectoral guidance if necessary, what parts of the puzzle are essential and how sharp a focus is necessary. A validation plan specifies both which parts of the puzzle must be assembled and the degree of focus, or effort, required.

During the course, it is intended that delegates should establish a validation plan for a typical method. The first workshop introduces the standard operating procedure for the method, the documentation available and considers differing requirements.

Outline

- Purpose
  - of method: what is the analytical problem?
  - of validation study: verification or validation?
- Performance criteria
  - what performance parameters are critical?
  - what values should they have?
- Test plan
  - how should the performance be measured?
  - how much experimentation is needed?
- Interpretation
  - how should the parameters be interpreted?

A documented validation plan must include a number of elements.

Central to the process is the purpose of the exercise. It must be completely clear what the analytical method is intended to achieve, and what the validation is intended to achieve. In considering the latter, it is useful to consider whether the study is intended to demonstrate adequate performance against a requirement (validation) or performance up to a standard already demonstrated (verification); verification of the performance of a previously validated method requires significantly less effort.

Ideally, the end use should imply a performance requirement in terms of trueness, precision, detection capability and robustness. Even where this is not the case, it is often possible to establish some guideline figures for performance. These figures amount to a performance specification.

Given a ‘specification’, it becomes possible to plan a set of tests to establish adequate performance. It may be possible to estimate the required power of the tests from a consideration of risk; more commonly, general practice, industry or other guidelines give an indication of the tests required.

Finally, the results of each test need interpretation. In some cases, this may be a simple comparison of performance statistics, often aided by statistical testing. In others, evaluation may require independent review or even independent expert review. It may also be necessary to specify methods of dealing with poor experimental data.

Workshop B1 (Part 2)

Plan precision, bias and ruggedness studies

- Precision
- Repeatability
- Intermediate precision
  - Two analysts
  - Different days
- How many concentration levels?
- Which samples to analyse?
- How many groups of data/replicates per group?
- Target values for precision?
- Data analysis

Workshop B1 (Part 2)

- Bias/recovery
- No matrix certified reference material
- Which materials to analyse?
  - how many matrices/analyte levels
- Target value for recovery?
- How many replicates?
- Data analysis

Workshop B1 (Part 2)

- Ruggedness
- Which parameters to study?
- Values for each parameter in study?

Workshop B1 (Part 3)

Plan selectivity, capability of detection and working range studies

- Selectivity
  - how to assess?
- Detection limit
  - is it important for this method?
  - what sample to analyse?
  - which 'multiplier'
- Linearity/working range
  - concentration range?
  - how many levels?