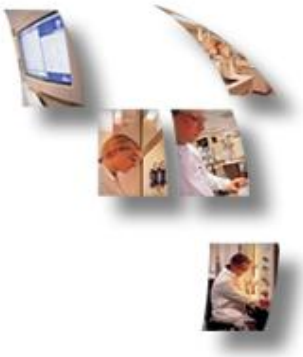

Partial validation - when is enough enough?

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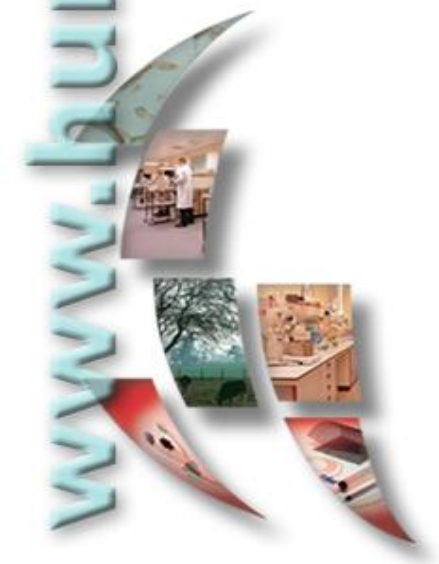
16-18 November 2011



Overview

- Discuss some commonly occurring situations covered by partial validation section of the EMA Guideline
- Topic highlighted as no clear standards outlining extent of experiments required
- Suggest a more harmonised approach to certain types of partial validation

Background

- 2001 FDA Guidance defined different categories of validation:
  - Full validation
  - Partial validation
  - Cross validation
- Concept carried forward to EMA Guideline

Partial validation

- Partial validation is a useful tool but there are a number of commonly occurring situations where the concept results in different approaches taken to validate methods
- Consensus rather than prescriptive changes

Why a common approach is required

- Sound science
- Regulatory acceptability

Common scenarios

- Transfer of a fully validated method to another laboratory
- Method fully validated in one species - validate method in second species
- Changes in validated calibration range
- Validations in tissues

Method transfer

- Considerations - experience working with method, new analytical platforms and analysts, method complexity
- Key experiments:
  - Matrix effects, selectivity
  - Stability - use data generated during original method validation or repeat?
  - Precision and accuracy - how many batches?

Validate method in second species

- Things to consider:
  - Different analyst?
  - How much experience working with method?
  - Timings?
- Key experiments:
  - Matrix effects, selectivity, stability
  - Precision and accuracy - how many batches?

Change of calibration range

- Original range 1 to 1000 ng/mL
- New range 0.5 to 500 ng/mL
  - Within and between batch precision and accuracy?
  - Selectivity and matrix effects

Tissues

- Increasing number of TK studies include tissue samples
- Expectation that tissue methods are validated to same standard as plasma methods
- How much validation?
  - Stability in tissue homogenates?
  - Extent of precision and accuracy experiments?

Conclusion

- Do not want to be prescriptive, but certain common situations need a harmonised approach
  - Method transfer - full validation including stability
  - Validation in a second species - key analytical parameters including within and between batch precision and accuracy
  - Changes in calibration range outside validated range - evaluate within and between batch precision and accuracy
  - Tissues - method qualification only