

Feedback from Workshop:  
“Qualification and Validation of  
Analytical Methods: is the cost  
worthwhile?”

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# Qualification vs. Validation

- Most companies use Qualification instead of Validation of analytical methods at the early stage of drug substance and drug product development (Phase I, Phase IIa)
  - Full Validation is required for late Phase II and Phase III programs
- Qualification is viewed as a Validation in Progress
  - Methods are generally tested only for linearity, specificity, solution stability
- A Qualification Report documents method development
  - Developmental work is summarized in a brief section for Qualification vs. extensive section for Validation
- Wide use of Generic Methods
  - TFA HPLC methods are preferred to allow easy transition to LC-MS (impurities/degradation Products screen)
  - Use of chromatography modelling softwares (e.g. DryLab) for method development
- Qualification is time and cost-saving compared to a full Validation and is considered acceptable by WW external Regulatory Agencies for Phase I/early Phase II clinical studies. Some education might be required for internal Regulatory functions.

# Can Instrument Qualification/Validation avoid redundant Method Qualification/Validation?

- Instruments performances are regularly verified (6-monthly or annually)
- Instrument parts are also regularly replaced
- Generally used System Suitability criteria:
  - 6/5 replicates injections of standard solution (precision of injection)
  - 50% and check standard solution injection
  - Specificity solution (e.g. 0.1% standard solution)
  - Bracketing of sample solutions
  - Impurities/degradation products solution
  - Column performance (efficiency, plate count, tailing factor, etc)
- Although it was felt that most System Suitability criteria needs to be verified, it was generally agreed that the new generation of HPLC provide enough robust performances to possibly eliminate the need to check precision of injection at each analysis

# Use of Qualification & Validation Data

- Set uncertainty of analytical results
  - e.g. Linearity data can be used to determine uncertainty on weights
- Set specifications for methods' transfer

## Validation of Compendial Test Methods

- Clear guidances for qualification/validation of compendial procedures (e.g. titration or TLC) not available
- Is full validation required for minor modifications of a compendial method (e.g. use of a different salt form) ?
- Suggested criteria:
  - Check Reproducibility of the test method
  - Test of the method at 2 or more different concentrations