

GLP in the Bioanalytical Lab – An Intended Purpose Approach from Good Science towards Compliance.

By Christopher Tudan, Ph.D.

The intended purpose of this section of the program is to provide in-depth training on the “Intended Purpose” approach to Bioanalytical Method Development and Validation as supported by the recent Crystal City meetings and pertinent white papers. I will lead (and support) discussions on the currently accepted concepts and criteria for the development and validation (or qualification) of bioanalytical methods that are GLP/GCP compliant. Specific case studies and raw data examples are used to illustrate method development strategies and successful implementation of validation efforts towards rapid and compliant validation processes that are conducive to robust and efficient sample analysis. Although the focus of the discussions will be LC-MS/MS directed, examples and important perspectives on the validation of Ligand Binding Assays will also constitute an important component of this section. Additionally, sample preparation considerations will be discussed because of the impact it has on batch repeats and signal background and interferences. Finally, effective approaches to the technical review of raw data, including the acceptance and rejection of data, will be utilized towards the end of the course to cement the points considered earlier in the day.

Program Outline:

1. FDA Guidance Recommendations for Method Validation.
2. Validating a Bioanalytical Method:
 - a. Method Validation performance characteristics
 - b. Validation experiments
 - c. Validation criteria – Today’s standards (current expectations)
 - d. BA Validation parameter requirements – Addressing test requirements and criteria of each Validation experiment
 - e. Reference Standards
 - f. System Suitability
 - g. Incurred Sample Re-analysis.
3. Validation Report Components.
4. Partial versus Cross Validations – Changes in Validation Parameters versus Respective Minimal Experimental Requirements and Criteria.
5. Method Development – Recommendations/Strategies to Facilitate a Rapid and Compliant Validation Process.
6. Bioanalytical Study Plans.
7. What Should You Be Looking for in the LC-MS/MS Raw Data? - Interpreting Chromatography, Scans, Spectra, Response Measures and Method Parameters that Impact the Data.
8. LBAs - Recommendations for Fitting Non-linear Calibration Curves, Selectivity, Pre-study Validation versus In-study Validation, Specific Nonselectivity versus Nonspecific Nonselectivity (i.e., Assessing Parallelism).
9. Sample Preparation Consideration in Method Development for Speed/Accuracy/Quality.
10. Acceptance / Rejection of Data.
11. Technical Review of Raw Data.
12. Final Discussions and Exchange of Experiences and Perspectives.