Bioanalytical Assay:

Bioanalytical assay/Bioanalysis is one of the key elements part of generic pharmaceutical industry which involves with the quantitative measurement of drugs and/or their metabolites in biological fluids e.g. blood, plasma, serum, tissue extracts or urine. Bioanalysis plays a significant role in evaluation and interpretation of pharmacokinetic and bioequivalence studies. It frequently involves the measurement of drug in biological matrix at very low concentration levels, typically at ng/mL. With this emphasis, a sensitive and selective bioanalytical method is essential. A modern analytical instrument e.g. LC-MS/MS is widely used for bioanalysis since it offers excellent sensitivity, selectivity, accuracy and precision.

Generally, a bioanalytical method consists of three phases as follows:

1. Bioanalytical method development

The main purpose of method development is to design the suitable experimental conditions including sample preparation process and the condition of measurement. To achieve a suitable, accurate, precise and reliable method, the sample preparation techniques such as protein precipitation (PP), liquid-liquid extraction (LLE) or solid phase extraction (SPE) are typically used to clean up a sample before analysis with LC-MS/MS. Additionally, other factors that may affect an accuracy and reliability of analysis, including protein binding, back-conversion, inhomogeneity, matrix effect and insource breakdown of labile metabolites, are also studied and evaluated during method development. This phase is the step to develop and produce “fit for purpose” assays from developed phase to the fully validated assays.

2. Bioanalytical method validation

Before a bioanalytical method can be implemented for routine use, it must first be validated to demonstrate the performance of the method and the reliability of the analytical results. The validation parameters which are listed in the US-FDA and EMA guidelines on bioanalytical method validation including selectivity, carry-over, lower limit of quantification, calibration curve, accuracy, precision, dilution integrity, matrix effect and stability should be fully validated. After validation of all parameters is completed, the developed method can be used for the intended bioanalytical application.

3. Samples analysis

After completing the full validation of the bioanalytical method, the method can be implemented for measurement of drug or metabolite in biological samples e.g. blood or urine of volunteers. The results of bioanalytical data are used for evaluation and interpretation of pharmacokinetic, bioavailability and bioequivalence studies between the test and reference products.

As mentioned above, all phases of bioanalytical assay (i.e. method development, method validation and study sample analysis) must comply with the Good Laboratory Practice (GLP) regulations according to the European Medicines Agency (EMA) and United States Food and Drug Administration (US-FDA). Therefore, this can be ensured that the bioanalysis results are accurate, precise and reliable.

References

1. Guidelines for the Conduct of Bioavailability and Bioequivalence Studies. Drug Control Division, Food and Drug Administration, Ministry of Public Health, 2009.
2. Guideline on Bioanalytical Method Validation. European Medicines Agency, Science Medicines Health, Committee for Medicinal Products for Human Use (CHMP), July 2011.
3. Guidance for Industry: Bioanalytical Method Validation, U.S. Department of Health and Human Services Food and Drug Administration, Center for Drug Evaluation and Research (CDER), Center for Veterinary Medicine (CVM), May 2001.