Wide Spread use of LC-MS in Bioequivalence Studies

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Before the first bioanalytical method validation workshop, there was lack of uniformity in conducting validation of bioanalytical methods and submission of data to regulatory agencies. The bioanalytical validation workshop in 1990 was the first major workshop dedicated to investigating and harmonizing procedures in method validation. The workshop was cosponsored by the American Association of Pharmaceutical Scientists (AAPS), the US FDA, the International Pharmaceutical Federation (FIP), the Health Protection Branch (HPB), and the Association of Analytical Chemists (AOAC). The conference focused on the requirements for bioanalytical method validation procedures to establish reliability of the analytical method, parameters to ensure acceptability of analytical method performance, method development (prestudy validation), and method application (in-study validation). The workshop defined important parameters for method validation e.g. accuracy, precision, selectivity, sensitivity, reproducibility, limit of quantification as well as addressing “how to” evaluate and determine these parameters. It was also clarified that it is not essential to have 100% recovery, but it is important that the recovery be reproducible. One of the most important outcomes of the first workshop was that it defined “the acceptance criteria for a run”. The recommendations of the first workshop were well received within the scientific community. These recommendations did not become did not become official until the draft guidance on bioanalytical method validation was published in January 1999 by the US FDA with the intention of seeking public opinion prior to finalizing the guidance. The second bioanalytical method validation workshop was cosponsored by the AAPS and the US FDA in January 2000 a year after the draft guidance went into effect and ten years after the first workshop took place. The main advances occurred in the field of mass spectrometry. Two issues were addressed in relation to LC-MS; interference from substances that are physico-chemically similar to the analyte (e.g. metabolites, endogenous compounds, interference from matrix components unrelated to the analyte (matrix effect) [2]. In the case of LC-MS-MS based procedures, appropriate steps should be taken to ensure the lack of matrix effects throughout the application of the method, especially if the nature of the matrix changes from the matrix used during method validation [3]. Different type of validation was defined, namely: partial validation, cross validation, and full validation [2].

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