S12-2 Pharmacometric approach to optimizing pharmaceutical formulations

◯Kozo TAKAYAMA[1]

[1]Hoshi Univ.

The ICH Q8 guidelines have necessitated the establishment of a science-based rationale and the “Quality by Design” concept has been advocated in the pharmaceutical formulation development. The characteristics of drug products are influenced by a number of causal factors related to pharmaceutical formulations and manufacturing conditions. In recent years, statistical approaches such as response surface methods (RSM) have been used for seeking acceptable formulations of pharmaceuticals. However, predictions based on linear regression models are often limited and the results obtained occasionally exhibit poor estimation. To overcome these difficulties caused by linear regression models, a novel RSM incorporating a multivariate spline interpolation (MVS) was developed to generate smooth and natural response surfaces, and thereby to estimate a highly accurate optimal solution. Concurrently, a method to evaluate the reliability of the optimal solution was newly developed employing a bootstrap re-sampling technique (BS) and a Kohonen’s self-organizing map (SOM). Predominant feature of a novel RSM approach based on MVS together with BS and SOM was demonstrated by the design and optimization for several pharmaceutical products. In these model formulations, reasonable optimal solutions were successfully determined. It would be unable to reach the exact combination of causal factors using a normal analysis based on a one-factor-at-a-time experiment.