

A General Method for Optimal Design of Univariate and Multivariate Population Pharmacokinetic Experiments

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ABSTRACT

We will present a general method for optimal design of univariate and multivariate population pharmacokinetic experiments. Expressions for population Fisher information matrix have been defined for univariate and multivariate pharmacokinetic experiments and a major assumption often made is that variance-covariance matrix of the interindividual variabilities has only diagonal elements so that whenever off diagonal elements are present, they must be ignored during the design of a future experiment. Recently expressions that accounted for these off diagonal elements were developed for univariate population pharmacokinetic experiments, this work has extended these to multivariate population pharmacokinetic experiments. These expressions were applied to a population pharmacokinetic/pharmacodynamic example. The results obtained showed that optimal designs are different with and without off diagonal elements and ignoring the off diagonal elements can lead to a design that produce more biased and less precise parameter estimates compared to a design that include the off diagonal elements.