

Experimental Design for Pop b

by

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Abstract

Researchers have been using the standard empirical design to select blood sampling times for obtaining Pop-PK parameters, which has lack of systematic evaluation and optimization. D-optimal design has been a useful tool for designs of experiments applied mostly to manufactory processes. It has been recognized and adapted by pharmacometricians in the recent years. We propose a practical approach that links the D-optimal design with Pop-PK modeling so that the quality of PK parameter estimation is a function of design: the number of concentrations measured per subject, the timing of each blood sample, and the number of subjects. This approach can be executed in two stages: First, a preliminary/historical study is done to estimate the Pop-PK model. Second, a D-optimal design is employed based on the Pop-PK model to optimize blood sampling times for future PK studies, such as DDI studies.

Simulations showed that the optimized sampling times enable us to draw fewer blood samples without sacrificing the precision obtained with a standard empirical design.

This was joint work with Bo Jin, Nancy Agrawal and Alan Hartford.