

## **Abstract**

A broad approach to the design of phase I clinical trials for the efficient estimation of the maximum tolerated dose is presented. The method is rooted in formal optimal design theory and involves the construction of constrained Bayesian c- and D-optimal designs. The imposed constraint incorporates the optimal design points and their weights and ensures that the probability that an administered dose exceeds the maximum acceptable dose is low.

Results relating to these constrained designs for log doses on the real line are described and the associated equivalence theorem is given.

The ideas are extended to more practical situations and specifically to those involving discrete doses. In particular, a Bayesian sequential optimal design scheme comprising a pilot study on a small number of patients followed by the allocation of patients to doses one-at-a-time is developed in a user-friendly software package.