

Simulation Tools for Optimal Designs

Collaborative Research Yields Better Adaptive Trial Designs

Response-adaptive trial software simulates early phase studies to determine the best design

Challenge

Adaptive trial designs are driving a smarter, more flexible era in clinical development. Yet this increased flexibility — the ability to refine the design after the trial has begun — presents trial sponsors with the added problem of deciding which design options are best for a particular study.



Recently, one of the top five global pharmaceutical firms sought to simulate response-adaptive trials to better understand the “trade-offs” between various designs.

There were no suitable commercial software packages. The company turned to the experts at Cytel to help complete the methodology research then custom design and deploy a statistically valid, computationally practical solution.

The resulting tool simulates a wide variety of adaptive trial design types, some utilizing compute-intensive Bayesian methods. With the deployment of the simulation tool, project biostatisticians and their clinical team colleagues are now determining adaptive trial design strategies faster and more accurately.

“Working together with Cytel allowed our team to move from research to reality with a swiftness not possible without Cytel. We now have the tools to help guide our innovative trial design decision-making efficiently and intelligently”

- Vice President, Early Stage Biostatistics”

Statistical Expertise and Software Innovation Combine to Produce Adaptive Trial Simulation Tools

Response-adaptive designs provide clinical teams with more flexible, efficient, and ethical ways to conduct dose-finding studies. By adapting the allocation rules through the course of the study, more data is amassed on doses eliciting desirable response levels, thereby increasing the likelihood of choosing correct doses for confirmatory clinical testing.

Response

- Cytel organized a cross-functional team of biostatisticians and application engineers and worked with the client to develop their original concept into a comprehensive functional specification.
- In close collaboration with the client's biostatistical and IT staff, the Cytel statistical team conducted research to identify, refine and optimize several methods for simulating dose-adaptive studies.

Adaptation

- Cytel optimized and implemented a number of dose-adaptive methods including "up-and-down" designs, the Continual Re-assessment Method (CRM), and Bayesian model-based designs. Most Bayesian approaches incorporated sophisticated Markov Chain Monte Carlo (MCMC) algorithms.
- An easily-understood Multiple Document Interface (MDI) allowed concurrent simulations of several trials with differing dose levels, dose response variances, etc. Simulation results were placed in a relational database for fast retrieval and comparisons.

Outcome

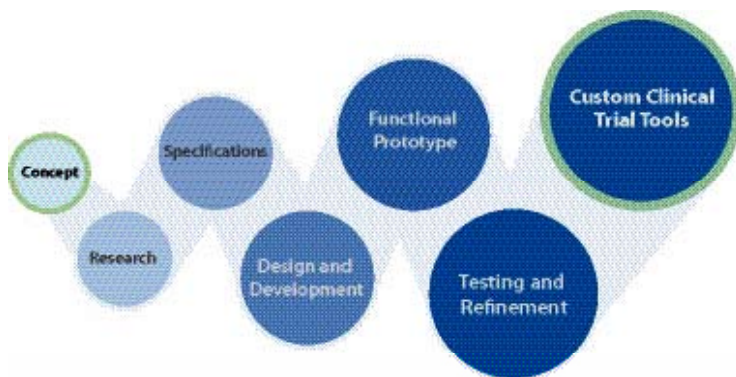
- A single, integrated software solution allowed the client's trial design and clinical teams to simulate and compare various adaptive design scenarios. Cytel's parallel computing environment provided much faster design choice assessments.
- The client received a 21 CFR Part 11 compliant randomization solution for real-time deployment in dose-adaptive trial designs.
- Trial planners attained a clear picture of the operational "trade-offs" of each adaptive design option. The sponsor's clinical team and project management now compares the operating characteristics of each study, predicting recruitment patterns and drug supply dynamics.

The Cytel Advantage

Trial simulations are now helping companies assess the performance characteristics of various adaptive design options. Simulation results also provide compelling evidence supporting regulatory approval of the proposed trial.

In research organizations of all sizes, Cytel's validated and open technology solutions enable trial planners to determine the best design for both early and confirmatory studies. With a unique combination of biostatistical expertise, top-flight programmers and deployment experience, Cytel Pharmaceutical Research Services collaborations make clinical trial innovation practical.

Developing the Tools of Clinical Innovation



Cytel Pharmaceutical Research specializes in the custom tools that drive meaningful clinical R&D innovation such as study simulators, dynamic randomization solutions and Bayesian-based trial design tools.

Employing an Integrated Software Development Methodology (ISDM) model, Cytel statisticians and software engineers collaborate closely with their sponsor team counterparts while complying with internationally-accepted standards.