Berry Consultants
Statistical Innovation

FACTS

FACTS Fixed and Adaptive
Clinical Trial Simulator V6.1

# The Leading Edge of Trial Design

FACTS is a software system for simulating clinical trials, enabling biostatisticians to optimize and fully understand the trial design through the simulation process. FACTS was designed with input from leading industry biostatisticians and is licensed by major pharmaceuticals companies, CRO's and Biotechs, and over 20 academic and research organizations.

FACTS enables 'in silico' trial design. Through detailed and complex trial simulation, the statistician has a "flight simulator" in which they can simulate a variety of different trial conditions and scenarios, creating a much more thorough understanding of the trial design's strengths and weaknesses, which through this Insilco process allows for constructing a very efficient and strong design.

## The FACTS Engines

The FACTS simulation engines are grouped into 4 types: Dose Escalation designs, FACTS "Core" designs where 1 or more treatment arms are tested against one or two control arms, Enrichment designs where the same treatment is tested in different patient populations or different indications and "Staged" designs where FACTS simulates two trials that are run back to back such as a Phase IIA and Phase IIB, or Phase II and Phase III. FACTS simulates the decision making between the stages and can simulate them as separate trials or a single seamless trial.

All the engines are fronted by a common user interface (UI) that makes FACTS easy to learn and easy to use. As well as ease of use, FACTS is feature rich, flexible, fast and delivers extensive outputs and graphical summaries.

## Feature Rich

FACTS has innovative features in each engine:

**Dose Escalation**: 3+3, mTPI, CRM, CRM targeting a toxicity band, 2D-CRM, overdose control, single subject run-in, categorical toxicity, toxicity and efficacy, continuous enrolment, fine-grained dose selection, multiple dose escalation controls, multiple stopping rules.

**Core Designs**: Dose response modeling, longitudinal models, hierarchical priors for control, dose response adaptation, Bayesian and frequentist analysis, Bayesian predictive probabilities and user defined quantities of interest to be estimated in the MCMC sampling.

**Core Multiple Endpoint**: A particularly powerful extension to the Core design simulators is the ability to simulate, analyze and act on up to four endpoints. These might be efficacy and tolerability endpoints, early and late endpoints, or primary and secondary efficacy endpoints or any combination of these.

**Enrichment Designs**: Hierarchical response modeling across the control arms and the estimate of the treatment effect, hierarchical priors for controls, longitudinal models, study and sub-group level adaptation.

**Staged Designs**: Simulate the treatment selection at the end of a phase and the decision whether to run the next stage or not and the impact this has on the next phase.

## Flexible

FACTS is flexible – all these options are individually selectable and can be combined with the other options. This makes the range of study designs that FACTS can simulate enormous, but it also means that working in FACTS, a trial designer can build a trial design up incrementally starting with a straight forward design and exploring the impact of innovations one at time, and selecting the best.

## Fast

The trial simulators are all tightly coded in C++ and run 10-100 times faster than designs created within statistical programming environments. For many designs 1,000 simulations can be run in a few minutes or even seconds. We can also support licensees integrating FACTS with their computing grid facilities for running very large numbers of simulations of particularly demanding designs. Being able to get simulation results quickly transforms the experience of designing complex trials.

## Full Output

The user has full access to all the simulation results including the final analysis of each simulated trial, every interim analysis of each simulated trial, and all the simulated subjects and their responses within each trial. The results are written out into CSV files that are easily loaded into other analysis tools. FACTS has extensive graphical support, allowing the simulation results to be visualized and easily presented including allowing the user to walk through the simulation of individual trials.

## Detailed Simulation

FACTS allows detailed specification of the simulated data to be sampled and passed to the design as the trials are simulated – properties such as the overall dose response, patterns of longitudinal responses, recruitment rates and dropout rates can all be specified. Allowing designs to be specified, simulated, and analyzed in minutes rather than days.

It is also possible to load into FACTS a database of externally simulated subject responses, allowing the clinical team complete control of the simulated patient population, allowing, for instance, the simulation of responses based in PK-PD models.

## Design Variants

FACTS makes it easy to compare the performance of a design at different sample sizes, not just comparing the type-1 error and power but also the design's ability to make correct decisions such as selection of the best dose and identification of the correct treatment population or indication.

## Analysis

All the engines now support analysis of an externally provided dataset as well as simulation of trials. Giving a new way to evaluate designs and making it easier to use FACTS to implement the trial that has been designed.

## A Platform for the Future

For designing adaptive trials, FACTS offers an unparalleled access to innovative trial design ideas, it is being actively developed by an expert team at Berry Consultants, overseen by our senior statisticians and advised by our licensees.