Clinical Trial Simulation

Pharsight Trial Simulator

Nick Holford
Dept Pharmacology & Clinical Pharmacology
University of Auckland, New Zealand

Who Started This?

Camilla (Maruszewski) Olson
Creative Director at Camilla Olson LLC
San Francisco Bay Area, Apparel & Fashion

“Who Started This?”

29 Jan 2012

History of Pharsight

• Pharsoft founded by Camilla Olsen in early1996
  – Name still used by Pharsight (Jan 2012)

Pharsoft Corporation
125 University Ave, Palo Alto, CA 94301
p 757-720-1450
http://www.pharsoft.com

• Idea proposed by Carl Peck to Camilla Olsen when attempts to commercialize NONMEM with Beal & Sheiner fell through

• Pharsight “Trial Designer” was originally based on a simulation engine licensed from the Right Dose First Time (RIDO) project which was developed at the University of Auckland (Nick Holford)
Amazing Marketing

**Trial Design**

Pharsight Trial Designer, requirements: Pentium 90, 32 MB, SVGA monitor with 800 x 600 pixels and 256 colors, CD-ROM drive (required for installation), 32-bit Windows operating system (Windows 95, 98, NT 3.51, or 4.0), 16 MB RAM for 95, 20 MB for NT 3.51, and 32 for NT 4.0, Microsoft Visual C++ 4.2 for NT 3.51 or 5.0 for NT 4.0 or 95 to create user-defined model components and to link to SAS, PC SAS version 6.12 or later installed as an OLE automation server; $7500, special educational pricing available; MountainView, Calif., Pharsight Corp, 888-708-7444, info@pharsight.com.

**Introduction: Drug Development is a Bigger and Bigger Business.** The average cost of a compound is now $300 million, and the clinical trials to get the drug approved are complex and costly. This is not a program to open nonchalantly. It requires a change of mindset and a commitment to learn. Are two days worth the investment in planning a better study? For small studies, perhaps not, but for large studies, and, perhaps more importantly, for a sequence of studies, this sort of structured thinking can only improve the quality of studies. It does not replace the need for a statistician to help decide which design is appropriate. There is no intelligent help to aid you in deciding which design is needed for which phase of the research program.

---

**A Key Insight from Lewis Sheiner**

**More than One Model!**

- **Covariate Distribution Model**
  - Distribution of age, sex, renal function, etc.
  - Create simulated "individuals"
- **Input-Output (Drug Model)**
  - Mechanistic (PKPD) preferred
  - Individual and Observation stochastic elements
- **Nominal Protocol Model**
  - The ideal world
  - Patients, treatments, observations
- **Trial Execution Model**
  - Compliance, dropouts, missing samples
  - Costs

---

**What is the Trial Simulator?**

[Diagram of Trial Simulator]

- **Clinical Trial Plan**
  - Covariate Distribution Model
  - Specification of the Virtual Trial Population
  - Drug Model (Population) Distribution
  - Nominal Design (Population) Distribution
  - Clinical Adherence
  - Data Analysis Plan

---


The Covariate Model

The Drug Model

The Nominal Design Model
The Protocol Deviation Model

Target Concentration Controlled Trial

Drug Model


Target Concentration Controlled Trial

Nominal Design Model