QUANTIFY THE PROBABILITY OF SUCCESS IN CLINICAL RESEARCH
MAKE BETTER DECISIONS ON DRUGS

Software for adaptive design and Bayesian decision analysis

DECIMAKER™

What is Decimaker?

Decimaker is an innovative statistical software for the adaptive design and the Bayesian decision analysis of clinical trials. Pharmaceutical and biotechnology companies use Decimaker to design and simulate adaptive trials. With Decimaker, they estimate in real-time the probability of success in the study, and adjust its course accordingly. A user-friendly graphical interface enables to simulate, compare and analyse dose-ranging studies using a comprehensive set of Bayesian analysis, allocation and decision procedures.

Why is it important?

Pharmaceutical companies want to accelerate the development of novel therapies, making better go/no go decisions and selecting doses faster. They want to terminate failed compounds sooner to allocate resources to most promising agents. The want to avoid failed studies by making sure that each dollar invested in a trial will generate decision-enabling information. Adaptive designs and Bayesian methods permit a dynamic monitoring of clinical research, controlling the information collected towards decision making. Decimaker helps pharmaceutical decision makers to get the best return on investment by maximizing the quality of clinical data and minimizing information gathering costs.

Who should use it?

Decimaker is designed for analysts, technical experts and deciders involved in pharmaceutical clinical trials. In a single interface, it integrates a complete trial design and simulation platform, Bayesian analysis capabilities and a decision-enabling toolbox. Adopting new software across a large organization can be challenging. That is why Decimaker offers all capabilities in the same package, making it easy for you to work as a team on a trial project and to move it along from the design to the implementation stage.

Under the FDA critical path initiative, pharmaceutical companies are adopting new strategies to bring innovative medicines to the market.

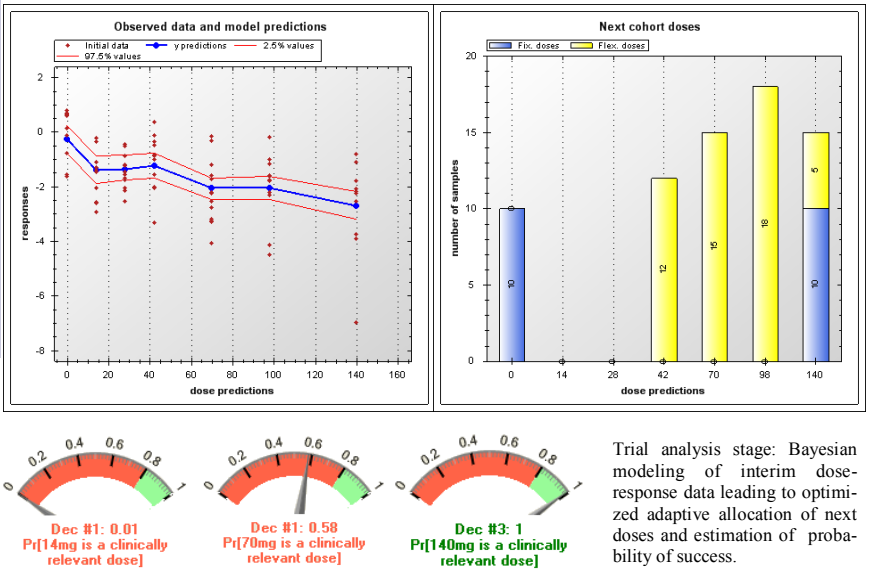
Using adaptive design and Bayesian decision analyses, the return on clinical research investments may be much improved, leading to better go/no go decisions, faster dose selections and avoiding failed studies.

Decimaker software from Clinbay brings powerful Bayesian adaptive design and decision analysis methods to the pharmaceutical professional desktops.

Designed to assist clinical development teams during protocol design, study implementation and analysis, Decimaker handles innovative adaptive designs, complex Bayesian analysis and decision-making solutions with a user-friendly graphical interface. Decimaker is an optimized and comprehensive solution to drug development .

With Decimaker, you enjoy the full power of R and OpenBUGS statistical analysis programs enhanced with a tailored process flow and graphical interface that simplifies your work.

Decimaker simulation and analysis results are visualized graphically to assist decision makers to quantify probability of success and take the best decision for their drugs.



Trial analysis stage: Bayesian modeling of interim dose-response data leading to optimized adaptive allocation of next doses and estimation of probability of success.

ClinBAY
statistical solutions to drug development

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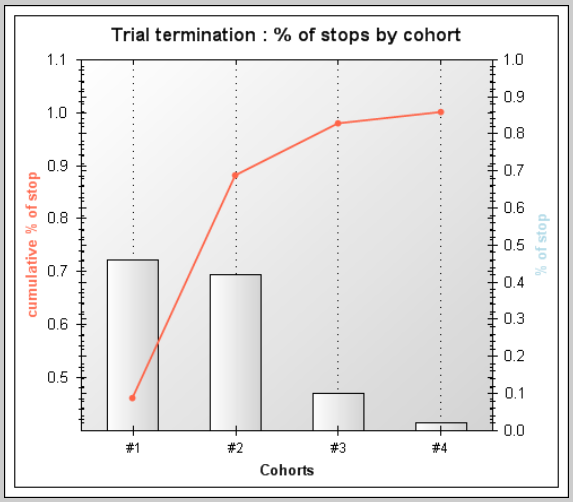

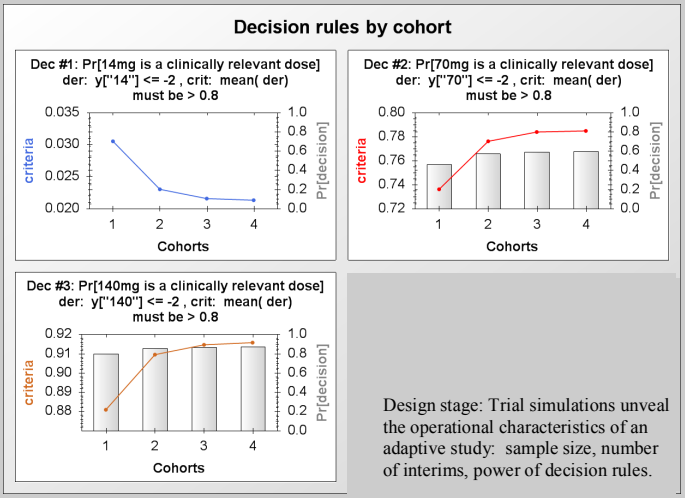

Design stage: Trial simulations unveil the operational characteristics of an adaptive study: sample size, number of interims, power of decision rules.

If you are a company executive, decision maker, physician or project manager, you will appreciate to get reliable, data-driven and objective summaries of probability of success for your projects. You will also monitor how these numbers evolve across multiple scenarios and as trial investments are made. You will make better decisions at the end, relying on all data that was available to you, and adjust strategies as evidence gets objectively collected. The use of Decimaker by your drug development teams will help you to gather faster decision-enabling knowledge and to influence the success of your company.

As a technical expert in trial design and analysis, you are always striving towards a better way to conduct clinical research. You are concerned about design efficiency, optimized analysis methods and minimization of risks and costs. You know how to do it, but your time is often limited and must be shared across multiple teams that request your help. Using Decimaker, you have access to modern Bayesian modeling capabilities for various types of data. You will construct and assess adaptive design scenarios based on innovative Bayesian allocation algorithms: CRM, response variance, D– or C-optimal. You will define decision rules and measures of risk and success that meet the trial objectives. After a simulation-based assessment of various options, you will deliver the best solution to your customers for trial implementation. All of these tasks may be done very fast, thanks to the graphical user interface of Decimaker. As needed, you may export projects for additional customized processing in SAS, R or Winbugs.

As a trial analyst, you are valued for the on-time delivery of quality analyses and decision-enabling reports. When implementing adaptive designs, the need for interim analyses of data increases your work load and shortens timelines. The use of Decimaker will simplify your tasks greatly and improve quality. The analysis plan is defined upfront at the trial design stage. The whole plan may then be locked, with methods being documented and programs being created and validated. Decimaker provides flexible data-reading capabilities and locking features to control integrity. Decision-enabling reports are generated in tabular and graphical formats for a rapid integration into study reports, presentations or publications. Analysis logs may be saved to disk, enabling an audit trail of the work being accomplished.

Companies use Decimaker for:

- **Preclinical studies**

Several dose-ranging preclinical experiments are run for the discovery and selection of drug candidates. Using the Bayesian features of Decimaker, scientists may chain results across studies, leading to more reliable estimates of drug activity. Candidates may be prioritized and benchmarked against concurrent or historical, positive or negative controls using Decimaker.

- **Phase I safety trials**

First-in-human trials are carried out to estimate the maximum tolerated dose (MTD) and characterize the safety profile of new molecular entities. Compared to fixed-dose escalation methods, response-adaptive techniques, as available in Decimaker, such as the Continual Reassessment Method (CRM), bring you faster to the dosage range of interest, providing a precise and reliable estimate of the MTD. This produces direct ethical and financial benefits on the phase I plan. Impact on phase II/III plan is also significant, as one may rule out any under-dosing possibility when the MTD has been defined with confidence.

- **Biomarker studies**

Biomarkers are often used prior to the first efficacy study to assess drug-activity and guide the selection of doses for phase II.

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Biomarker outcomes are frequently driven by a known mechanistic model relating activity to dose or concentration. Decimaker offers a series of model-based adaptive design techniques, such as the Bayesian D-optimal models, to help scientists to deliver faster proof of mechanism responses and drug-activity relationships. The usage of these innovative techniques is greatly simplified by an intuitive and simple-to-use graphical user interface.

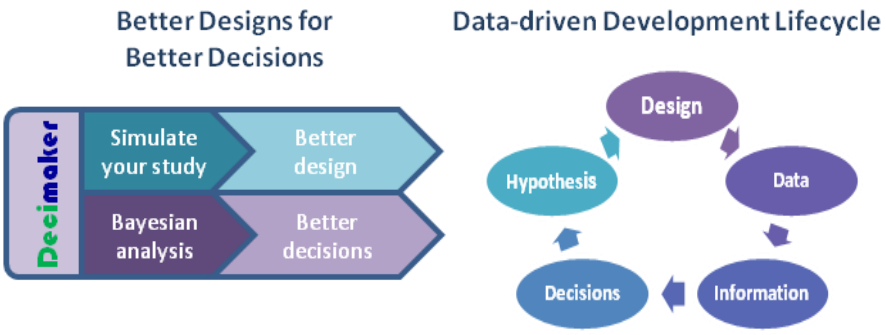
- **Phase II efficacy trials**

Proof-of-efficacy, evidence of dose-response and dose-selected for phase III are the three main objectives of phase II studies. Fixed-dose studies often fail to respond satisfactorily to all 3 goals because the retained dosage range is off-target or too narrow, or for lack of power. The adaptive dose-response design features of Decimaker provide you the flexibility to assess one objective after the other in a single trial. Doses are adjusted dynamically to the most informative range, producing sample size gains and avoiding study failures. The Decimaker simulation capability permits to study the operational characteristics of your pre-planned adaptive designs, so that trial integrity is guaranteed.

- **Phase III trials**

Decimaker is a specific and integrated software for adaptive design, trial simulation and analysis. It provides a comprehensive framework to facilitate your interactions with regulators.

Corporate and individual licenses for Decimaker are available by annual subscription. For more information visit our website at **www.clinbay.com** or contact our sale representatives at **info@clinbay.com**.



To better serve our customer needs, Decimaker is available in 2 versions:

Decimaker analytics

- Includes the data analysis interface with Bayesian model and decision rules.
- Ideal for study analysts and scientists analyzing their trials.

Decimaker pro

- Includes the analytics capacilities, the adaptive design methods and the trial simulation interface.
- Ideal for trial design and modeling experts and for advanced decision makers.

" From a 'big picture' view, drug development is a sequence of decision processes. To achieve the ultimate success, we cannot consider each trial as an isolated piece; instead, using Bayesian decision theory..."

Mark Chang, Ph.D.
Millenium Pharmaceuticals, Inc.,
Cambridge, Massachussets, USA
(in *Adaptive Design Theory and Implementation Using SAS and R*, Chapman et Hall/CRC, 2007).

"Adaptive designs must become the rule, not the exception for all new drug candidates entering in clinical testing. We have chosen the power and flexibility of Decimaker to implement this approach in our company"

Bruno Boulanger, Ph.D.
UCB Pharma SA
Braine-L'Alleud, BELGIUM

Design adaptive trials. Simulate studies to control their characteristics. Conduct Bayesian dose-response modeling and decision analyses. Decide with confidence. Select doses optimally.

All with Decimaker ™.

Decimaker generates R & OpenBUGS scripts for data analysis :

- Allow all users to get started quickly.
- Require no previous programming knowledge.
- Present point-and-click options: selection boxes, menus, formula and radio buttons.
- R (D)COM server running behind the Decimaker interface
- Produces R scripts for data processing, Bayesian analysis using BRugs and summaries.

Interactive graphics and summary tables that are generated automatically during analysis:

- Link points in a graph to data in the corresponding table for easy viewing.
- Produces easy-to-understand summaries for trial simulations and analyses.
- Generate adaptive randomisation tables and simulate next cohort of data, as you wish.

Bayesian analysis models are available for

- Binary and continuous endpoints
- ANOVA, linear and logistic regression, non-linear (e.g, Emax) and semi-parametric models (e.g.,Normal Dynamic Linear Model).
- Vast choice of prior distributions, including the normal, gamma,log-normal, beta, and many more…
- Ability to assess the impact of priors on model fit and to monitor/diagnose convergence.

Innovative response adaptive allocation methods that may be easily implemented and compared:

- Choose among several criteria the most relevant allocation method for your project: CRM, D-optimal, C-optimal, variance of target responses.
- Customize the allocation technique to benchmark your drug to a concurrent or historical, negative or positive control or a fixed threshold.
- Define flexibly the size and content of each cohort, being enrolled successively into the study: dose levels, fixed/flexible doses, sample size minima and maxima.
- Adjust the randomisation/allocation technique to your project needs: play-the winner, biased-coin, urm , or higest subset methods.

Efficient study workflow to share and construct projects among multiple contributors

- Modular integration of data, modeling, adaptive allocation, decision and trial simulation components.
- One-click transition of a project from the « design » to the « implementation » stage.
- Instant sharing of project files (*.dcm) including design plans, data and analysis results using import/export facilities.
- Ability to lock data and analysis plan modules, upon approval of study protocol.
- Import and visualize standard data files (text, Excel and comma-separated formats).

Learn and compare the operational characteristics of various trial proposals using simulations

- Many trial scenarios may be constructed, including data simulation plans, analysis methods, allocation and decision rules.
- Multiple-part studies are possible, considering custom decision-trees to go from one part to the next.
- Simple to interpret tabular and graphical display of power curves, sample size, allocation summary, model adjustment and relative efficiency to a standard design.
- Simulate-at-interim capability to quantify predictive power of various options and make the best decision.

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statistical solutions to drug development