



**ADDPLAN**

Adaptive Designs – Plans and Analysis

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The indispensable tool for the design,  
simulation, and analysis of clinical trials

# ADDPLAN - The indispensable tool for the design, simulation, and analysis of clinical trials

Comprehensive, user-friendly, fully validated, CFR 21, Part 11 compliant



Based on extensive experience in designing and analyzing confirmatory adaptive trials, ADDPLAN released the first version of the package in 2002 - the first and only package worldwide for adaptive design, simulation, and sample size recalculation at the time.

With release 5 MC (Multiple Comparisons), **ADDPLAN** is the first software package that incorporates multiple comparison procedures for multi-armed adaptive trials, including treatment selection designs, flexible combination of clinical research phases, and population enrichment designs. The majority of the requirements brought forward in the FDA “Draft Guidance on Adaptive Design for Clinical Trials for Drugs and Biologics” are covered by **ADDPLAN 5 MC**.

*“Group sequential statistical design and analysis methods have been developed that allow valid analyses of interim data and provide well-recognized alpha spending approaches to address the control of the Type I error rate (e.g., O’Brien-Fleming, Lan-DeMets, Peto methods) to enable termination of a study early when either no beneficial treatment effect is seen or a statistically robust demonstration of efficacy is observed.”*

*“Studies with multiple groups (e.g., multiple-dose levels) can be designed to carry only one or two groups to completion out of the several initiated, based on this type of futility analysis done by group. (...) However, because of the multiplicity arising from the several sequential interim analyses over time with multiple between-group analyses done to select groups to discontinue, statistical adjustments and the usual group sequential alpha spending adjustments need to be made in this case to control Type I error rates.”*

*(FDA Draft Guidance on Adaptive Design for Clinical Trials for Drugs and Biologics)*

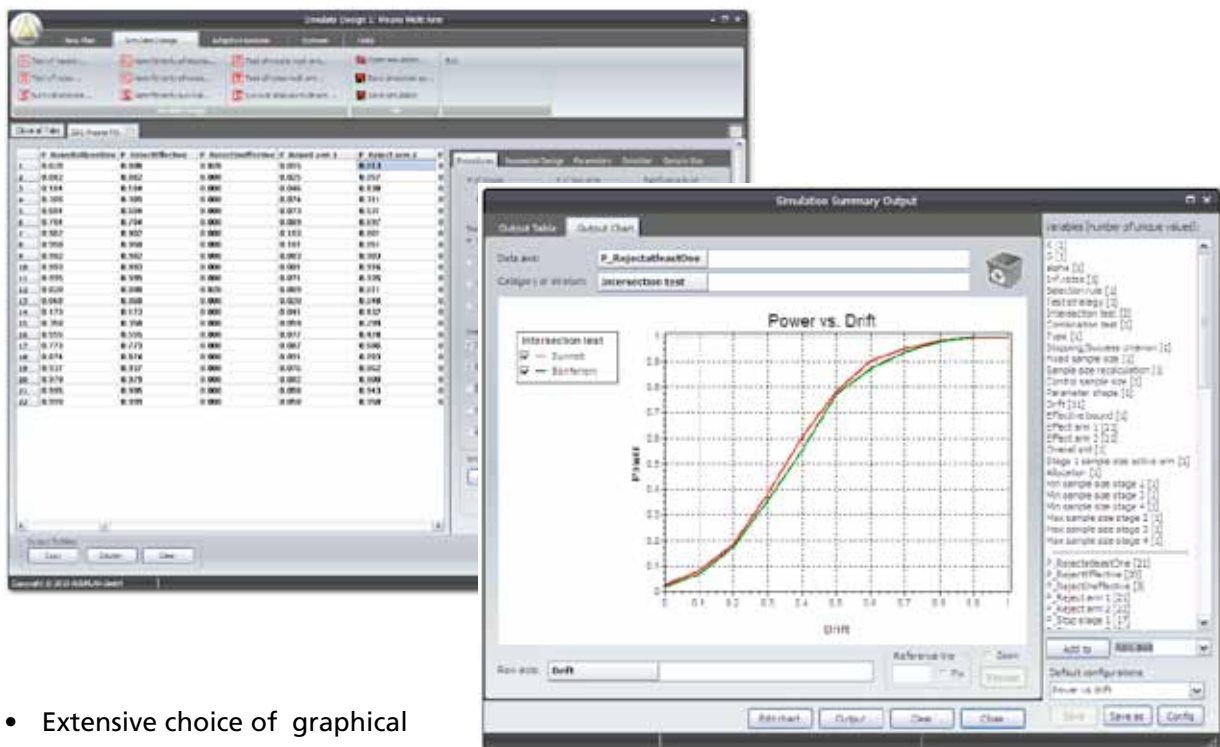






## Powerful Simulation Engine - You will be amazed how fast and accurate it is!

- Compare flexible combination tests with separate phase II/III designs
- Sample size reassessment procedures for multi-armed designs
- Assess the power and ASN of adaptive designs
- Assess the bias of effect size estimates
- Assess the probability to select specific treatment arms
- Choice of intersection tests: Dunnett, Bonferroni (Holm), Šidák, Simes (Hommel), hierarchical testing
- Comparison of treatment arm selection rules
- Comparison of dose-response shapes, e.g., linear, logistic, Emax, sigmoid Emax, exponential, etc.



- Extensive choice of graphical illustration of simulation results
- Easy processing of output table



## Adaptive Re-Design and Analysis

- Inverse normal method, Fisher's combination test, conditional Type I error approach, classic group-sequential
- Adaptive sample size recalculation
- Likelihood function and conditional power plot
- Repeated confidence intervals and p-values
- Confidence intervals and p-values by the end of the trial
- Multiple comparison procedures for multiple treatment arms
- Multiplicity adjusted confidence intervals for many-to-one comparisons

	Stage 1	Stage 2	Stage 3	Stage 4
Critical values reject Ho	6.883	7.863	7.337	7.824
Critical values accept Ho	-	-	-	2.824
Information rate	0.25	0.5	0.75	1.0
alpha spent	0.0001	0.0021	0.0106	0.0253
Overall global test statistic	0.790	0.933	1.778	-
Single stage p-value T1	0.2055	0.1505	0.0440	-
Single stage p-value T2	0.1862	0.2962	0.0196	-
Overall test statistic T1	0.754	1.264	2.017	-
Overall test statistic T2	1.747	1.467	2.585	-
95% CI T1	[0.455; 0.810]	[0.290; 0.453]	[0.008; 0.424]	-
95% CI T2	[0.401; 0.674]	[0.108; 0.471]	[0.052; 0.454]	-
Overall p-value (non-adapt) T1	-	-	-	58.2/50.2 [88.8%]
Overall p-value (non-adapt) T2	-	-	-	34.8/34.8 [88.8%]
Planned n1/0 (Power)	-	-	-	58.2/50.2 [88.8%]
Planned n2/0 (Power)	-	-	-	34.8/34.8 [88.8%]

**Test Result**

Stage 3:  
Based on the observed effect of this stage, the global null hypothesis cannot be rejected since the observed inverse normal test statistic does not exceed the critical level.  
By use of the closed testing procedure, some of the single hypotheses concerning treatment arm effects can be rejected.

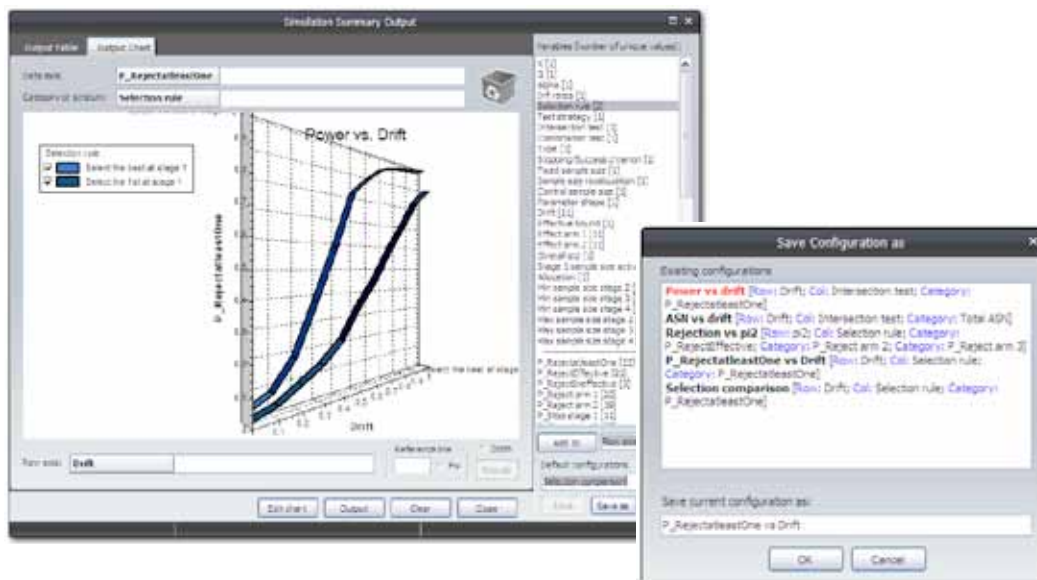
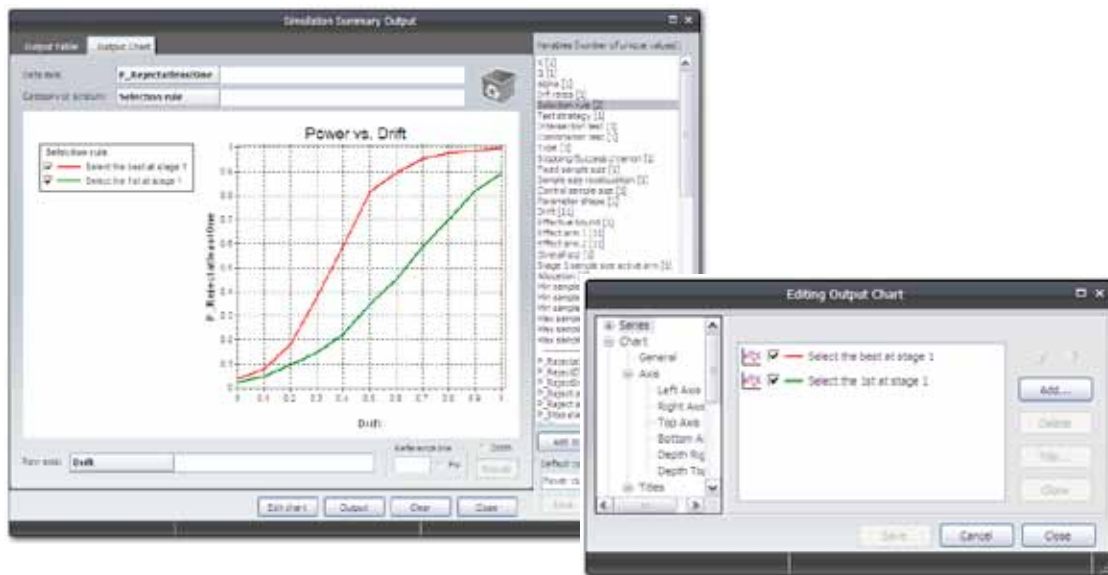
**Treatment arm 1**  
A sample size of n = 50.2 (control treatment group) and n = 50.2 (treatment group 1) is necessary to achieve conditional power 80.0% for the subsequent stage of the study.  
The power calculation is based on the observed overall response rates which are given by 0.454 and 0.461, respectively.  
Optionally, these values can be changed.

**Treatment arm 2**  
A sample size of n = 34.8 (control treatment group) and n = 34.8 (treatment group 2) is necessary to achieve conditional power 80.0% for the subsequent stage of the study.  
The power calculation is based on the observed overall response rates which are given by 0.454 and 0.461, respectively.  
Optionally, these values can be changed.

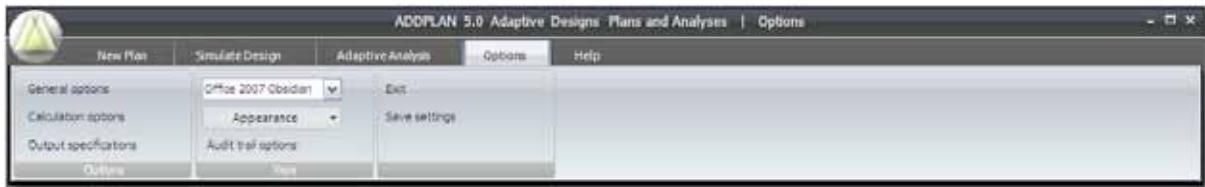
- Predefined text modules for interpretation of study outcome
- Extensive choice of graphical illustration of study results



## Customize your graphs and create your own configurations

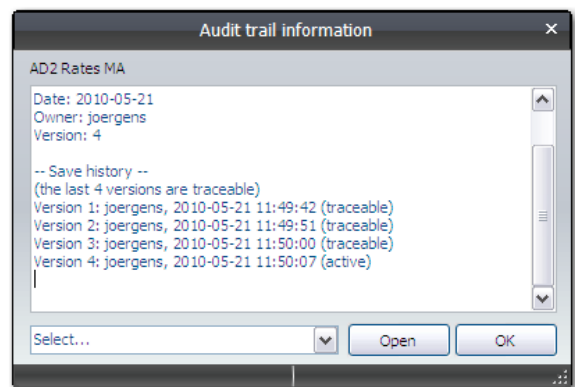
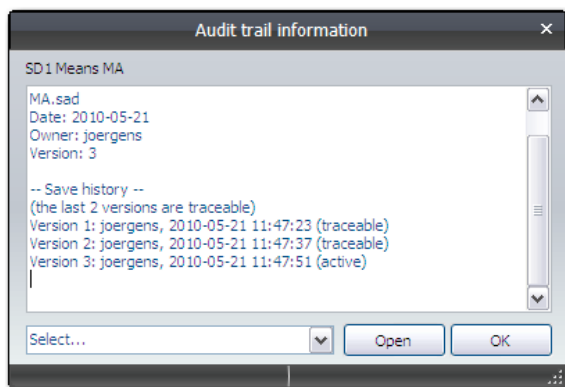


- Export graph as Bitmap, JPEG, Metafile, PDF, PNG, or PostScript
- Export table data as text, XML, HTML, or Excel



## General Features

- Server version available. Ask for our enterprise solutions!
- XML file storing system
- File versions audit trail





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