

Documentation for the program PRT_Sims.exe

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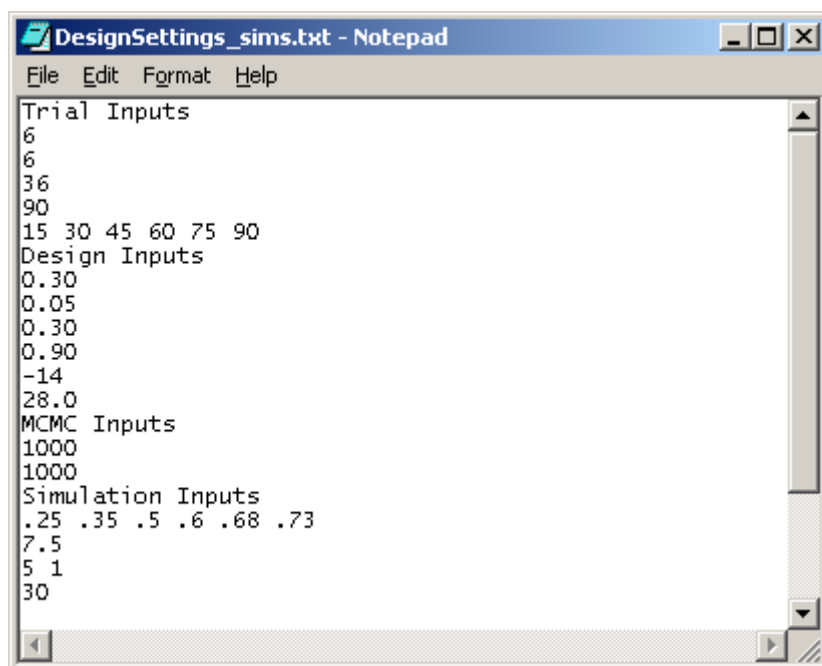
Overview

This readme file is intended to explain the inputs and outputs for the program “**PRT_Sims.exe**” that implements simulations for “Monitoring Late Onset Toxicities in Phase I Trials Using Predicted Risks” by Bekele, Ji, Shen, and Thall. The input file associated with this program is named “**DesignSettings_Sims.txt**.” Proper formatting of the **DesignSettings_Sims.txt** file is vital for appropriate execution of the program. The input file should be in the same folder as the compiled executable program **PRT_Sims.exe**. The output file generated from **PRT_Sims.exe** is named **out_sims.txt**.

This program runs on the Microsoft Windows operating system. Please send comments, suggestions and information concerning programming bugs to bbekele@mdanderson.org.

1. Description of DesignSettings_Sims.txt File

The following screenshot is an example of an appropriately formatted **DesignSettings_Sims.txt** file:



```
DesignSettings_sims.txt - Notepad
File Edit Format Help
Trial Inputs
6
6
36
90
15 30 45 60 75 90
Design Inputs
0.30
0.05
0.30
0.90
-14
28.0
MCMC Inputs
1000
1000
Simulation Inputs
.25 .35 .5 .6 .68 .73
7.5
5 1
30
```

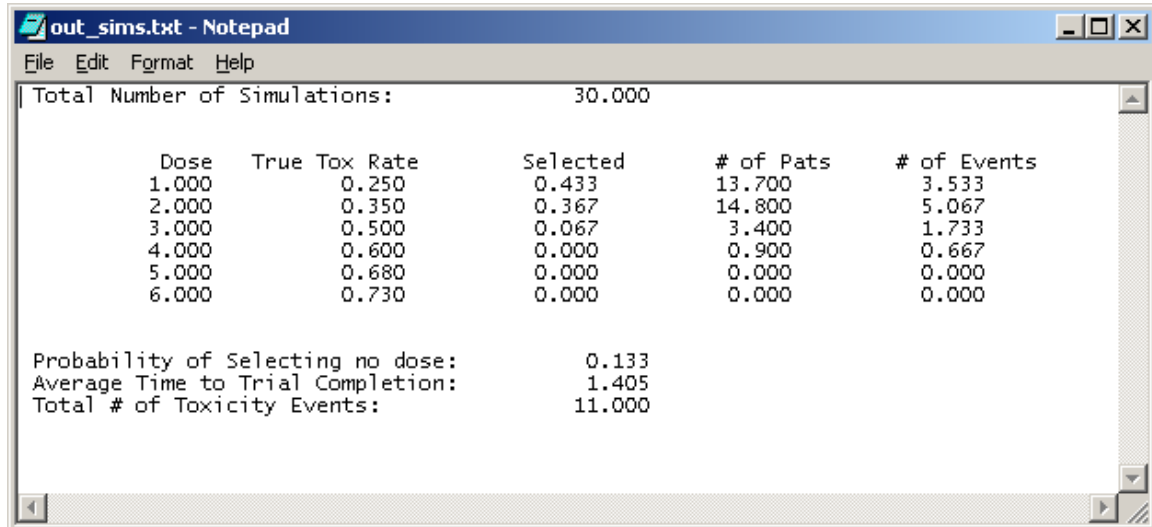
An explanation of the above screenshot is found in the Table below. The **DesignSettings_sims.txt** file is organized into 4 sections: 1) Trial Inputs; 2) Design Inputs; 3) MCMC inputs; and 4) Simulation inputs. We employ a color-coding scheme to explain these inputs. Text in red are the actual inputs. Text in black explains the purpose of each input. An

example **DesignSetting_Sims.txt** file is included when the **PRT_Sims.exe** file is download from the M. D. Anderson software download website.

Input Number	Example Input	General Description of Input
Trial Inputs		
1	6	Number of Discrete Time Periods. Denoted as C in the paper. Integer Input. Use integer values between 3 and 10.
2	6	Number of Doses. Maximum Number of Possible Doses is 10. Integer Input. Use integer values between 2 and 10.
3	36	Total Maximum Number of patients to enroll in the trial
4	90	Denoted by t^* in section 2.1 of the paper. Length of the assessment window in Days.
5	15 30 45 60 75 90	Denoted by t_j (for $j=2,\dots,C-1$) in section 2.1 of the paper. Time Intervals (in Days) used in the discrete time model of paper. Defined in Section 2.1 of the model.
Design Inputs		
1	0.30	π^* Target Toxicity Rate. This input must take on values between 0 and 1. Common values range between 0.20 and 0.35.
2	0.05	ε predictive probability cutoff used in decision rules 5 and 6. See paper for recommended values.
3	0.30	$\underline{\xi}$ lower posterior probability Cutoff used to define <i>negligible</i> toxicity. See paper for recommended values.
4	0.90	$\bar{\xi}$ Upper posterior probability Cutoff used to defined <i>excessive</i> toxicity.
5	-14.0	$\beta_{j,0}$ State-Space Model Prior mean for $\beta_{j,1}$. Assumed to be the same for all j .
6	28.0	σ_β^2 Prior variance of $\beta_{j,k} \beta_{j,k-1}$
MCMC Inputs		
1	1000	Number of initial iterations discarded as part of the MCMC algorithm. Known as the burn-in iterations.
2	1000	Number of iterations retained for estimation of the posterior after the burn-in iterations
Simulation Inputs		
1	.25 .35 .5 .6 .68 .73	True Probability of Toxicity by the end of the assessment window for each dose.
2	7.5	Inter-arrival time in Days. Average amount of time between accruals if suspending accrual were not allowed.
3	5 1	Hazard parameters which define if toxicities occur late, or early in the simulation. Denoted in Appendix B of the supplementary materials as α and β , respectively.
4	30	Number of iterations of the simulations

2. Outputs

Output generated by this program for the input file above is found in in 'out_sims.txt' and has the following format:



The screenshot shows a Notepad window with the following text:

Total Number of Simulations:		30.000			
Dose	True Tox Rate	Selected	# of Pats	# of Events	
1.000	0.250	0.433	13.700	3.533	
2.000	0.350	0.367	14.800	5.067	
3.000	0.500	0.067	3.400	1.733	
4.000	0.600	0.000	0.900	0.667	
5.000	0.680	0.000	0.000	0.000	
6.000	0.730	0.000	0.000	0.000	

Probability of Selecting no dose:	0.133
Average Time to Trial Completion:	1.405
Total # of Toxicity Events:	11.000

The output is organized to show, by dose (column heading "Dose"), the true toxicity rate used in the simulation (column heading "True Tox Rate"), Probability of Selecting the dose ("Selected"), average number of patients by dose ("# of Pats"), number of toxicity events ("# of Events"). Additional information includes the probability of selecting no dose, the average time to trial completion, and the total number of toxicity events. Note that the True Toxicity rate output will be exactly equal to Simulation Input 1 and the number of sims will be equal to the simulation input 4.

In this output 30 simulations were run. Since the target toxicity rate was 30%, as expected the method chooses doses 1 or 2 80% of the time. The average number of toxicities is 11 and the average time to trial completion is 1.4 years. A total of 13.3% of all simulations ended without selecting a dose because the model indicated that excessive toxicity had been observed.