Usage of the program

Download the executable program “phase12_win.exe”, and double-click it (or type the program name from the Windows command line) to run the simulation. The program will prompt users to input the following simulation parameters:

1) the number of dose levels for two drugs;
2) the true toxicity and efficacy probability for drug combinations;
3) the target toxicity (i.e., the highest acceptable toxicity rate);
4) the lowest acceptable response rate;
5) the prior estimates of toxicity and efficacy probability for individual drug;
6) the number of cohorts and the cohort size for phase I and II part of the trial;
7) the number of simulations.

When the simulation is done, results can be found in the file "results.txt" under the current directory.

Below is an example of the simulation for a two-drug combination trial (the numbers highlighted by red are parameters entered by users):

```
//////////////////////////////////////////////////////
//   Phase I/II design for drug combination trial    //
//         by Ying Yuan and Guosheng Yin             //
//////////////////////////////////////////////////////


please enter the number of dose for drug 1:  3
please enter the number of dose for drug 2:  2

Please enter the true toxicity probability for the combination (1, 1):  0.05
Please enter the true toxicity probability for the combination (1, 2):  0.1
Please enter the true toxicity probability for the combination (2, 1):  0.1
Please enter the true toxicity probability for the combination (2, 2):  0.15
Please enter the true toxicity probability for the combination (3, 1):  0.15
Please enter the true toxicity probability for the combination (3, 2):  0.2

 The true toxicity probability entered is :

Drug 2  2|       0.1      0.15       0.2
        1|      0.05       0.1      0.15
         --------------------------------
                  1         2         3
                     Drug 1

Are they correct ? (y/n):  y

Please enter the true response probability for the combination (1, 1):  0.1
Please enter the true response probability for the combination (1, 2):  0.2
Please enter the true response probability for the combination (2, 1):  0.2
Please enter the true response probability for the combination (2, 2):  0.3
Please enter the true response probability for the combination (3, 1):  0.4
Please enter the true response probability for the combination (3, 2):  0.5

 The true response rate entered is :
```

```
Drug 2  2|       0.2       0.3       0.5
        1|       0.1       0.2       0.4
         --------------------------------
                  1         2         3
                     Drug 1

Are they correct ? (y/n):  y

Please enter the target toxicity : 0.333

Please enter the lowest accpectable response rate : 0.2

Please enter the prior estimate of toxicity probability for drug 1 at the dose level
1:  0.05
Please enter the prior estimate of toxicity probability for drug 1 at the dose level
2:  0.1
Please enter the prior estimate of toxicity probability for drug 1 at the dose level
3:  0.2

The prior estimate of toxicity for drug 1 is: 0.05, 0.1, 0.2
Are they correct ? (y/n): y

Please enter the prior estimate of toxicity probability for drug 2 at the dose level
1:  0.1
Please enter the prior estimate of toxicity probability for drug 2 at the dose level
2:  0.2

The prior estimate of toxicity for drug 2 is : 0.1, 0.2
Are they correct ? (y/n): y

Enter the total number of cohorts for the phase I dose finding:  20

Enter the cohort size for the phase I trial:  1

Enter the total number of cohorts for the phase II trial:  60

Enter the cohort size for the phase II trial:  1

Enter the number of simulated trials:  1000

Are you sure to continue? (y/n): y


//////////////////////////////////////////////////////////////
// The simulation results can be found in the file results.txt //
// under the current directory when the simulation finishes.   //
//////////////////////////////////////////////////////////////

Simulating the trial 1......
Simulating the trial 2......
Simulating the trial 3......
Simulating the trial 4......
.
.
.
Simulating the trial 1000......
```

An example of the output file “results.txt”:

```
------------------------------------------------------------
Sun Aug 24 01:22:40 2008
CPU time (hour)= 0.54734 ;   the number of trials = 1000

Phase I cohort size = 1 ; the number of cohort = 20
Phase II cohort size = 1 ; the number of cohort = 60

Phase I dose-finding: escalate if pr(toxicity<0.333) > 0.8
                      de-escalate if pr(toxicity<0.333) < 0.45

A dose is admissible for phase II if 0.4<pr(toxicity<0.333) < 1

Phase II stopping rules: safety stopping if pr(toxicity<0.333) < 0.4
                         futility stopping if pr(efficacy>0.2) < 0.15

True toxicity:
       0.1      0.15       0.2
      0.05       0.1      0.15

True efficacy:
       0.2       0.3       0.5
       0.1       0.2       0.4


Number of patients treated at each dose:
    7.08     10.61     35.01
    6.78      6.62     12.57

Number of toxicity observed at each dose:
    0.71      1.60      7.07
    0.37      0.68      1.85

Number of response observed at each dose:
    1.44      3.26     17.40
    0.69      1.36      5.12

Selection probabilities (%):
    1.80      5.10     68.10
    0.00      1.80     21.30

Percentage of inconclusive trials: 1.90%
```