

Target Probability

Specifies the probabilities that determine the dose escalation/de-escalation/elimination rules for the trial:

Target Toxicity Probability (\emptyset): specifies the target toxicity probability of the maximum tolerated dose (MTD). Reasonable values are between 0.05 and 0.6.

BOIN specifies two alternatives, \emptyset_1 and \emptyset_2 , under which decision errors are minimized. Decision errors include escalating/de-escalating the dose when the current dose is above/below the MTD.

\emptyset_1 : the highest toxicity probability that is deemed sub-therapeutic (i.e. below the MTD) such that dose escalation should be undertaken. A default value of 0.6 x target probability is recommended. It is not sensible to set this lower bound very close to the target toxicity probability because the small sample size of phase I trial provides little power to detect a small difference (e.g., < 0.05) between two toxicity probabilities. Thus, probability values greater than 0.85 x target probability are discouraged.

\emptyset_2 : the lowest toxicity probability that is deemed overly toxic such that de-escalation is required. A default value of 1.4 x target is recommended. It is not sensible to set this upper bound very close to the target toxicity probability because the small sample size of phase I trial provides little power to detect a small difference (e.g., < 0.05) between two toxicity probabilities. Thus, probability values smaller than 1.15 x target probability are discouraged.

Select a method for determining MTD by clicking on its radio button in the **Find: (Single MTD or MTD contour)**. The single MTD option searches for a single dose pair that is closest to the target probability using an extension of the BOIN design to a 2-drug combination. The MTD contour option uses a waterfall design that divides the dose space into a number of subspaces and finds a separate MTD dose pair for each subspace, resulting in an MTD contour.