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 $0.6 \times$ 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 $0.85 \times$ 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 $1.4 \times$ 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 $1.15 \times$ 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.