

## Target Probability

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

**Target Toxicity Probability ( $\phi$ ):** specifies the target toxicity probability of the maximum tolerated dose (MTD). The textbox accepts any valid probability between 0.05 and 0.6.

BOIN specifies two alternatives,  $\phi_1$  and  $\phi_2$ , under which decision errors are minimized. Decision errors include escalating/de-escalating the dose when the current dose is above/below the MTD.

$\phi_1$ : the highest toxicity probability that is deemed sub-therapeutic (i.e. underdosing) 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.

$\phi_2$ : the lowest toxicity probability that is deemed overly toxic (i.e. overdosing) 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.