

## 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  $\phi_2$ , that are used to determine the optimal dose escalation boundary  $\lambda_e$ , and de-escalation boundary  $\lambda_d$  by minimizing the decision errors of dose escalation and de-escalation.  $\lambda_e$  and  $\lambda_d$  are the boundaries actually used to guide dose escalation and de-escalation. As there is a one-to-one correspondence, the software allows users to directly specify the desirable values of  $\lambda_e$  and  $\lambda_d$  while displaying the corresponding  $\phi_1$  and  $\phi_2$ .

$\lambda_e$ : the escalation boundary. If the observed DLT rate  $\leq \lambda_e$ , escalate the dose.

$\lambda_d$ : the de-escalation boundary. If the observed DLT rate  $> \lambda_d$ , de-escalate the dose.

$\phi_1$ : 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.