Overdose Control

Eliminate dose if $Pr\ (p_j > \phi \mid data) > P_E$,

where p_j is the true toxicity rate of dose level j, ϕ the target toxicity rate, and P_E the cutoff probability to eliminate an overly toxic dose for safety. We recommend the default value of $P_E = 0.95$ for general use. If the lowest dose is eliminated, the trial should be stopped for safety.

Check to impose a more stringent stopping rule on the lowest dose level:

$$Pr(p_1 > \ \phi \mid data) > P_E - \delta,$$

where p_1 is the true toxicity rate of the lowest dose (i.e., dose level 1), and δ is a small positive offset (between 0 and 0.1) subtracted from the cutoff probability. This rule says that if the lowest dose exceeds a certain safety threshold, we stop the trial for safety. A larger value of δ leads to a more stringent stopping rule. We recommend the default value of $\delta = 0.05$ for general use.

Check to ensure $\hat{p}_{MTD} \leq$ de-escalation boundary, where $\hat{p}_{MTD}$ is the isotonic estimate of the DLT probability for the dose selected as the MTD" allows to impose the condition: the selected MTD should have an isotonic estimate of toxicity probability less than or equal to the de-escalation boundary. This will improve safety, but at a slight sacrifice of selection percentage.