**iAdapt with nTTP – steps to trial simulation**

**Step 1: Specify parameter values**

* Weight matrix (W)
* Array of probabilities of observing AE grade for given dose, toxicity type (TOX)
* Number of toxicity types (ntox)
* The grade threshold at which an AE is called a DLT (grade.thresh)

**Step 2: Calculate “true” underlying dose-toxicity curve given inputs**

get.thresh()

Calculates mean nTTP at each dose level

dlt.prob()

Calculates DLT rate at each dose level

**Step 3: Specify hypotheses based on comparison to DLT rate**

**Step 4: Simulate trial(s)**

Stage 1

CALLS

CALLS

CALLS

CALLS

CALLS

Stage 1+2

nTTP.indiv.sim()

Calculates nTTP for one individual

tox.profile.nTTP()

Calculates LR for dose in Stage 1

\*inputs differ from original tox.profile()

safe.dose.nTTP()

Designates each dose as safe/unsafe

\*inputs differ from original safe.dose()

eff.stg1.nTTP()

Simulates Stage 1 (safety and efficacy)

\*inputs differ from original eff.stg1()

rand.stg2.nTTP()

Simulates full trial (Stages 1 and 2)

\*inputs differ from original rand.stg2()

sim.trials.nTTP()

Simulation wrapper

Note: this is a hierarchical structure, where each function calls only the one above it.