Supplementary Material

Analysis of biomarker utility using a PBPK model for carbaryl

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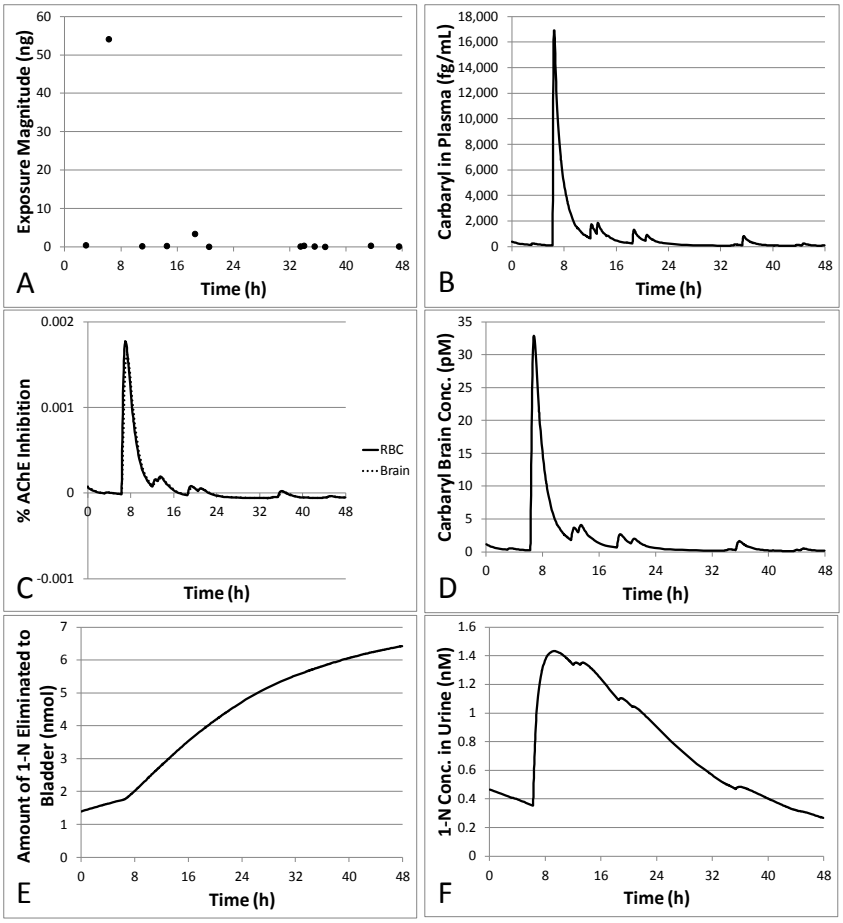
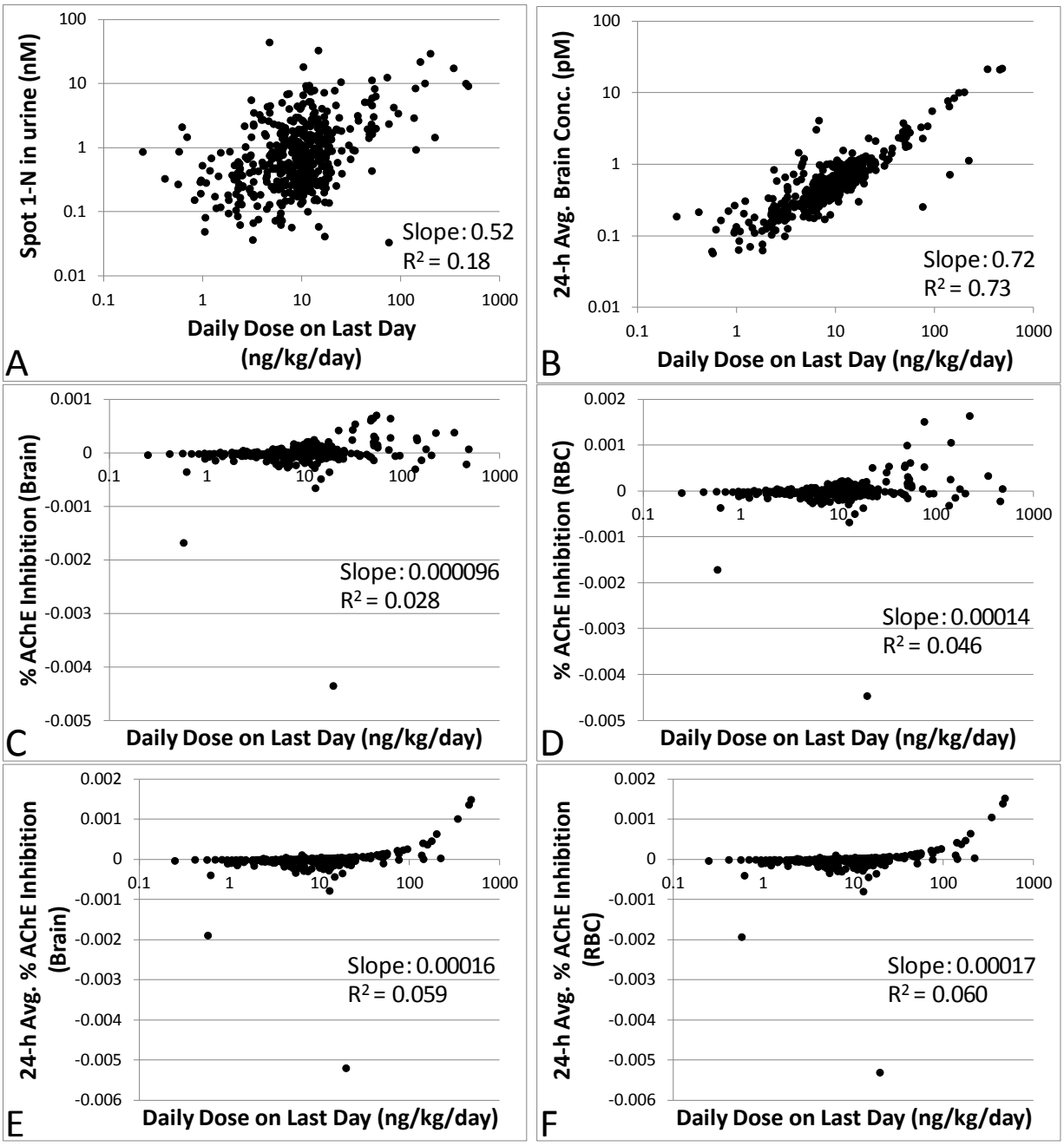


Supplementary Figure 1. Time course results for a single simulated individual over a 48 hour period. (A) Exposure magnitude (ng carbaryl); (B) concentration of carbaryl in plasma (fg/mL); (C) percent acetylcholinesterase (AChE) inhibition in red blood cells (solid line) and in brain tissue (dotted line); (D) concentration of carbaryl in brain tissue (pM); (E) cumulative amount of 1-naphthol (1-N) eliminated to the bladder compartment (nmol); (F) approximation of spot urine concentration of 1-N if the urine sample had been taken at a particular time point (rate of urinary elimination [nmol/h] divided by rate of urine output [L/h] approximates the spot urine concentration [nmol/L, or nM]).



Supplementary Figure 2. Correlations between six model-output variables and the total dose for the 24 hour period prior to the sampling time (ng/kg/day). (A) biomarker of exposure: spot 1-naphthol (1-N) in urine (nM); (B) target tissue concentration: carbaryl concentrations in brain averaged over the 24 hours prior to sampling (pM); (C) biomarker of early biochemical changes at the target tissue: percent acetylcholinesterase (AChE) inhibition in brain tissue (baseline = 0%); (D) biomarker of early biochemical changes at peripheral tissue: percent AChE inhibition in red blood cells (baseline = 0%); (E) percent AChE inhibition in brain tissue averaged over the last 24 hours prior to the urine sampling time; (F) percent AChE inhibition in red blood cells averaged over the last 24 hours prior to the urine sampling time.