

An AILI phenomenon of interest in liver lobules is the observation of extensive damage near the CV that spreads outward toward the PV over time. A mechanistic hypothesis is the zonation of the production of the reactant metabolite of APAP, NAPQI. Initial virtual experiments on AILI phenomena utilized an in silico analog of a mouse liver lobule. The primary AILI validation target was the observance of significantly more liver damage in Zone 3. This lobule analog previously achieved validation targets of APAP clearance with the inclusion of APAP metabolism. However, the downstream mechanisms from NAPQI formation to liver damage, and eventual necrosis, were not included. Therefore, mechanisms for GSH depletion and the production of “Damage” and “Repair” were implemented. The results of experiments using this modified lobule analog are described in Workflow Part 2 Part A and presented in the poster shown in Workflow Part 2 Part B.