



DILIsym is Quantitative Systems Toxicology (QST) software capable of **predicting** and **explaining** Drug-Induced Liver Injury (DILI)

Sound Science

- Developed through The DILI-sim Initiative, a consortium supported by 19 pharmaceutical companies and the FDA; regularly updated to include leading edge science
- Includes interacting sub-models such as: PBPK sub-model of drug disposition; bile acid representation of homeostasis and disruption by transporter inhibition; mitochondrial function and dysfunction sub-model including lipid metabolism and lipotoxicity; sub-model of oxidative stress generation and clearance; cell death representation of hepatocyte apoptosis, necrosis, and regeneration; representations of many well-accepted and novel biomarkers of liver injury
- Many publications released describing design and applications

Capable

- Utilizes compound-specific in vitro data to enable predictions
- · Humans, rats, mice and dogs included
- SimPops[™] incorporate inter-individual physiological variability
- User-friendly GUI for in silico experiments and visualization of results

Application Driven

- Rank candidates for DILI potential
- Extrapolate from animal and in vitro findings to humans
- Optimize clinical dose (risk versus presumed benefit)
- Infer magnitude of injury based on measured biomarkers
- Extrapolate from healthy volunteers to patient groups
- Guide incorporation of emerging biomarker measurements in clinical trials
- Analyze mechanisms underlying observed liver signals
- Inform choice and timing of biomarker measurements
- Aid identification of risk factors leading to precision medicine approaches

