DMPK

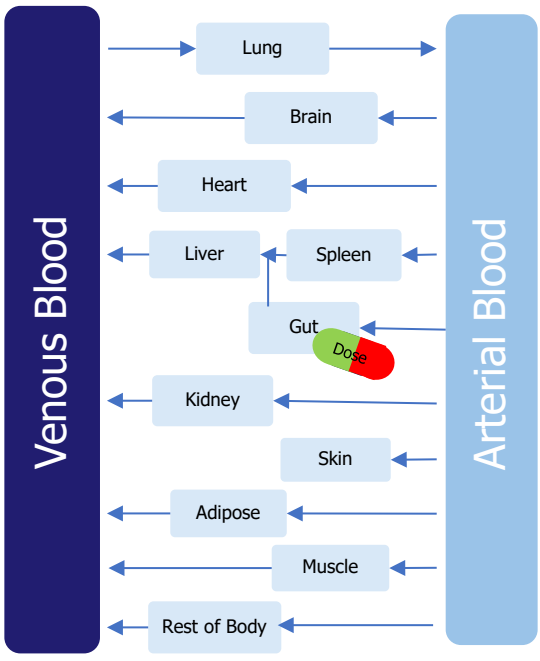
PBPK Modeling and Simulation

Pharmaron provides **Physiologically Based Pharmacokinetic (PBPK) modeling and simulation** services for predicting drug exposure in preclinical and clinical settings. PBPK enables **informed decision making** for efficacy, safety and dose prediction through lead optimization, candidate nomination and First-in-Human studies. By leveraging industry-standard GastroPlus software and Pharmaron's extensive drug development expertise, combined with our integrated experimental services, we deliver data-driven insights that foster innovation, instill confidence, and **accelerate your journey from concept to clinic**.

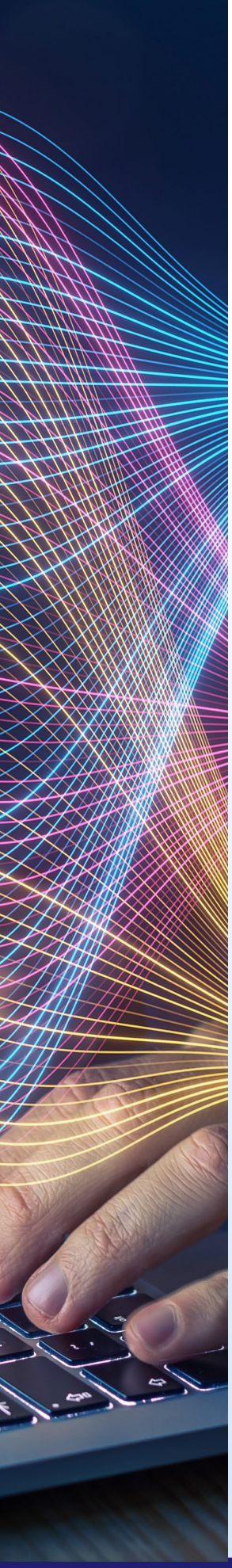
Model Informed Drug Discovery & Development

PBPK modeling and simulation provide a comprehensive, integrated data-driven approach that enhances decision-making, optimizes resources, reduces risk, and improves clinical outcomes.

- **Accelerate time-to-market** via simulations and scenario planning
- **Prediction of human PK,** including complex mechanisms
- **Maximize use of preclinical data** through effective *in vitro* to *in vivo* translation
- **Informed dosing strategies** for target engagement and pharmacology
- **Select optimal formulations** via mechanistic absorption models, linking physical properties with biopharmaceutic outcomes
- **Optimize delivery** to the site of action
- **Drug interaction prediction** and management
- **Predict clinical variability** across populations
- **Regulatory preparation:** all major global regulatory agencies now use PBPK models
- **Risk assessment** via simulation, giving critical insights into drug exposure



Mechanistic Absorption & PBPK Model



In-depth Analysis and Decision Making with Increased Confidence

Drug Discovery

- Get a mechanistic understanding of ADME processes in preclinical species and humans
- Verify distribution preclinically and predict for humans with increased confidence
- Optimize the drivers of absorption and systemic exposure
- Predict human PK & FTiH outcomes
- Estimate tissue concentrations at the target site of action
- Design PK/PD and safety studies with increased confidence

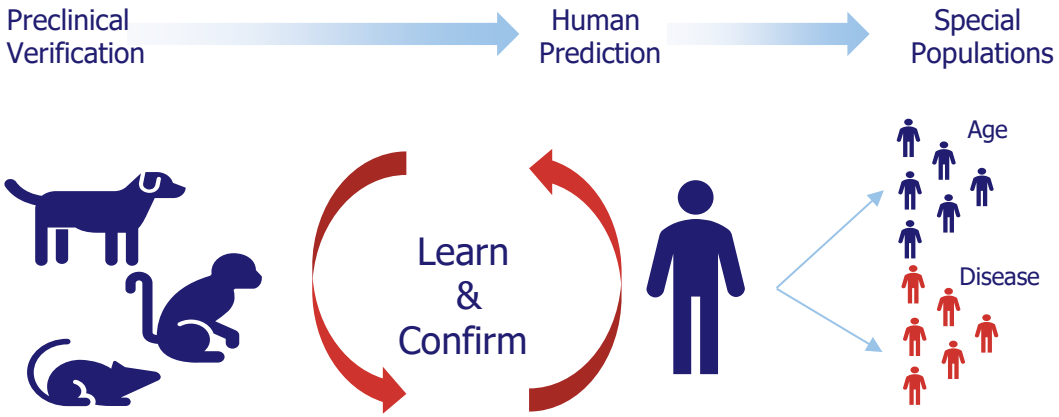
Lead Optimization / Preclinical

- Identify critical parameters through parameter sensitivity analysis
- Predict drug exposure in preclinical species
- Explore alternative routes of administration
- Evaluate biopharmaceutical properties and formulations
- Analyze food effects in animals and assess their implications for clinical treatment scenarios

IND-enabling / Clinical

- Extrapolate *in vitro* metabolism data to *in vivo* values (IVIVE) and predict human PK parameters
- Model FTiH and Phase I-IV studies
- Analyze Drug-Drug Interactions (DDIs) to evaluate the clinical impact of victim and perpetrator drugs

Learn – Confirm – Predict Cycle



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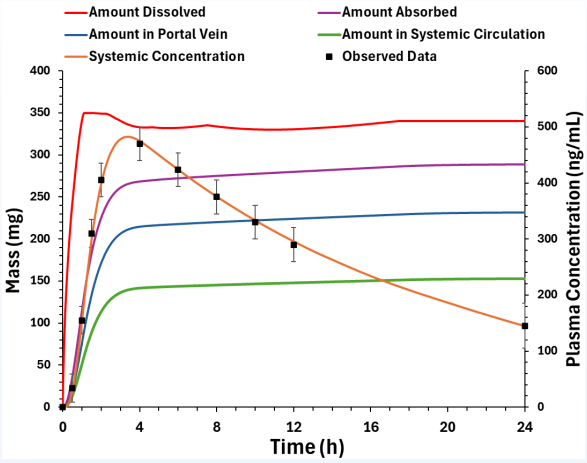
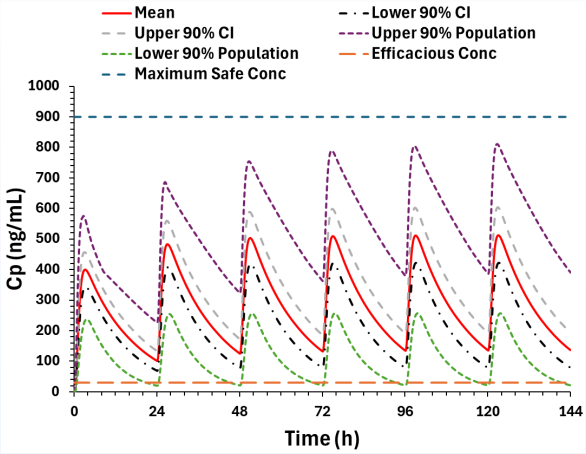
Combining PBPK Modeling with World Class ADME and *in vivo* Models to Advance Knowledge and Accelerate Timelines

Simulation Outputs

Dissolution/Absorption & Exposure



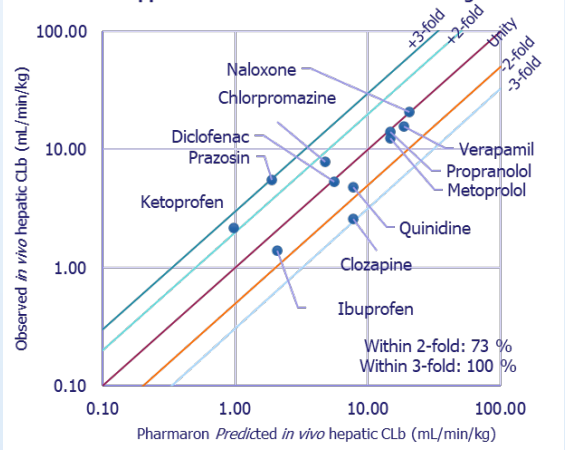
Efficacious Dose – Population Analysis



Optimized PBPK models can be used to investigate biopharmaceutical properties and simulate clinical dose regimens using different populations (disease/age). Human dose predictions are based on multiple factors such as the minimal efficacious target concentration and the maximum safe concentration. Population-based simulations indicate potential clinical variability.

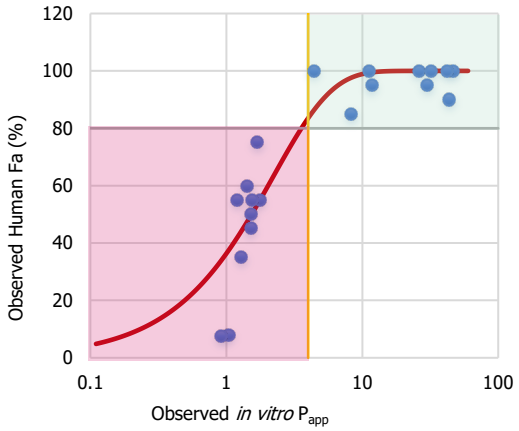
in vitro Assay Calibration

After application of the calibration and scaling



The predicted metabolic hepatic clearance (CL) for a panel of commercial compounds after applying an in-house calibration equation.

Absorption IVIVE (P_{app} to human F_a (%))



The correlation between *in vitro* permeability (P_{app}) and *in vivo* human fraction absorbed (Fa) enhances the accuracy of human absorption estimations.

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