

**Simcyp Simulator Platform**

- The Simcyp simulator is a computer software which uses mathematical models based on physiological processes in order to mechanistically predict drug disposition in the human population after oral, IV and dermal exposure.
- The simulator combines information on the physiological system with *in vitro* data on individual drugs to make predictions of plasma and tissue concentrations (Fig 1).
- By changing physiological information simulations in different populations (including elderly, pregnancy, paediatric populations) can be made

- Specific permeability limited disposition models are available to predict drug concentrations in the intestine. Kidneys, liver, brain, and lung (Fig 2).
- The lung model will be extended to mechanistically account for inhalational exposure as part of the project.
- A model of the blood:placenta will also be added to the simulator as part of the project.

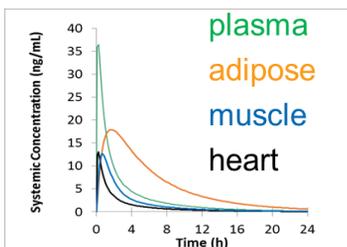


Figure 1: Prediction of drug concentrations in plasma and tissues

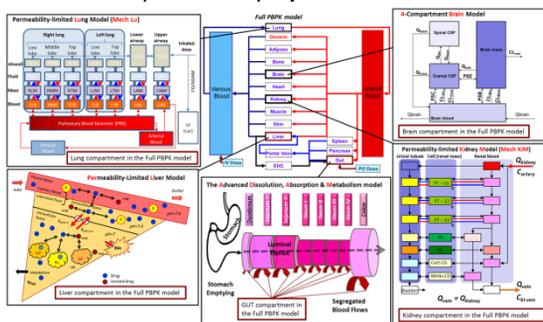


Figure 2: Schematic of the structure of the full-PBPK model available in Simcyp as well as the organs available to investigate permeability limited drug disposition

**Key contributions to EU-ToxRisk WP4**

Work package leader (Iain Gardner)

- To use simple PBPK models to allow reverse calculation from known toxic doses via plasma concentration to relevant nominal concentrations to be tested in *in vitro* assays (Task 4.1).
- To apply simple PBPK models for reverse dosimetry analysis to predict the human dose at which PoD occurs (Task 4.1).
- To generate detailed mechanistic PBPK models for compounds included in the case studies (Task 4.5).

**WP4 Milestones**

- MS21 – Collection of quantitative exposure data to parameterize PBPK models
- MS24 – Prediction of target site concentrations for first case study

**WP4 Deliverables**

- D4.2 – Human organ concentration predictions
- D4.3 – Reverse dosimetry report



**Key Simcyp personnel for EU-ToxRisk**

Dr Iain Gardner  
Senior Scientific Advisor and Head of Translational Sciences (DMPK)  
Leader of WP4

Dr Oliver Hatley  
Research Scientist, Translation Sciences (DMPK)

Dr Ciarán Fisher  
Senior Scientist, Translational Sciences (DMPK)