FROM VIRTUAL TO REAL

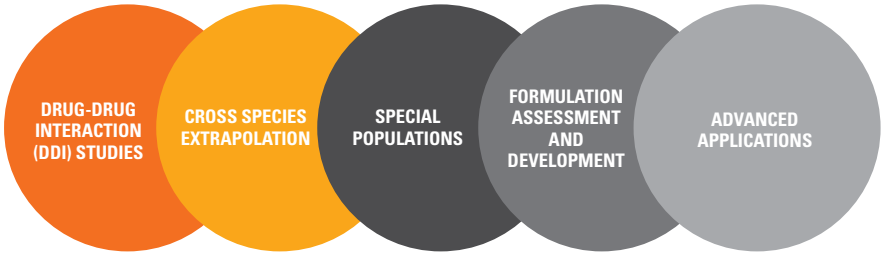
PHYSIOLOGICALLY BASED PHARMACOKINETIC (PBPK) MODELLING AND SIMULATION

Physiologically based pharmacokinetic (PBPK) modelling and simulation integrates prior knowledge and data generated through the R&D process to inform decisions for the next step of compound development, focusing on understanding and prediction of the absorption, distribution, metabolism and excretion (ADME) on targeted virtual populations.

WITH PBPK YOU CAN:

- Investigate drug concentrations at the site of action that may mechanistically drive pharmacodynamic effects
- Learn and confirm driven drug development as featured in current regulatory guidelines

PBPK ANALYSIS



SGS Exprimo uses the Open Systems Pharmacology Suite (containing PK-Sim® and MoBi®), which was developed by Bayer to set industry standards for efficient modelling and simulation. Now all pharma companies can leverage this PBPK technology via our expert SGS Exprimo consulting team to inform critical drug development decisions.

PBPK FOR DRUG-DRUG INTERACTION (DDI) STUDIES

Current regulatory draft guidelines from EMA and FDA testify the rise of PBPK applications in drug development and the increasing number of submissions. The majority (71 %) of these PBPK based submissions were related to DDI cases highlighting the importance in this field.

With PBPK you can:

- Accurately estimate complex DDI profiles of a compound in silico and explore its possible effects, e.g. on CYP and UGT metabolism as well as transporter liability before conducting a clinical study
- Use dynamic DDI simulations to predict the inhibitor effect at the site of metabolism (gut, liver, or any tissue) and estimate expected interindividual variability (90 % CI) for AUC and Cmax
- Fine tune your DDI study (number of subjects, minimal dose needed for quantifiable data, dosing schedule, effect of dose staggering, etc.) and avoid costly surprises

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- Investigate whether the exposure of a range of potential co-administered drugs is affected by the test drug prior to filing regulatory submissions with the FDA, EMA, and other agencies
- Enrich the data on your label and waive unnecessary clinical DDI studies for weak and moderate CYP-inhibitors or inducers

PBPK FOR CROSS SPECIES EXTRAPOLATION

PBPK models are highlighted in the new EMA guideline as a method for integrating relevant data before going to clinic to mitigate risks for the first in-human study.

With PBPK you can:

- Extrapolate knowledge from animal to human for drugs expected to have a narrow therapeutic window
- Easily change the physiology for extrapolations to another species and gain knowledge with more confidence from preclinical species to human
- Maximise information gain for first in class drugs and/or drugs with a limited therapeutic window
- Extrapolate in vitro metabolism and transport data to *in vivo* values (IVIVE) and predict exposures in animals and humans

PBPK FOR SPECIAL POPULATIONS

Being able to extract as much information as possible from limited data in diseased or special populations is essential in clinical development. PBPK models are the method of choice to predict drug behaviour e.g. in paediatric patient populations and perform clinical trial simulations for a paediatric investigation plan (PIP).

With PBPK you can:

- Extrapolate your results from healthy volunteers to vulnerable patient populations like new-borns and the very old
- Make population pharmacokinetic and pharmacodynamic predictions for different disease states and age groups
- Explore the physiological changes in diseased patients and the impact this has on the ADME of your drug
- Extract the most information from limited clinical data and bridge data gaps (from e. g. sparse sampling) with physiology information for informed decisions in drug development.

PBPK FOR FORMULATION ASSESMENT AND DEVELOPMENT

- Simulating virtual bioequivalence (BE) trials help you to optimise study design and formulation development
- Explore the ADME of your compound after administration via atypical application sites (e.g. lung inhalation, intramuscular, intranasal, etc.)

PBPK FOR ADVANCED APPLICATIONS

- The behaviour of small and large molecule combinations in models for antibody drug conjugates (ADC) can be investigated with PBPK modelling
- Multiscale modelling enables the investigation of drug concentration at a target site and thus support proof of concept studies which may explain the effect of concentrations at the target site

ABOUT SGS EXPRIMO

SGS Exprimo focuses on the application of population pharmacokinetic (PK), advanced PK/pharmacodynamic (PD) and drug-disease modelling & simulation to help decision making in drug development. With many years of experience and over 300 modelling and simulation projects performed, SGS Exprimo experts have also developed "Simulo", an in-silico modelling and simulation platform that facilitates complex clinical trial simulations. Simulo offers a modern software solution that implements PK, PD and disease progression models, run in an accessible, user-friendly, interface.

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WHEN YOU NEED TO BE SURE