Application of Modeling and Simulations at Different Stages of Drug Development

Modeling and simulation (M&S) are aimed at establishing models that provide guidance to support decisions in drug development such as trial design, efficacy/safety comparisons, dosage and/or regimen optimization, or endpoint analysis. M&S can be applied at any stage of the drug development program (from discovery to clinical) and facilitates decision-making and de-risking clinical studies in addition to delivering a faster and more accurate analysis of the trial results. Utilizing M&S can therefore reduce cost and shorten development time by optimizing the clinical assessment of safety and efficacy for human use.

The application of mathematical models at various stages of the drug development process is an active process that takes advantage of existing knowledge generated in both pre-clinical and clinical studies and helps integrate and utilize new information as it becomes available. Both the Food and Drug Administration (FDA) and the European Medicines Agency (EMA) recommend the use of modeling and simulation in the different phases of drug development and support its use by providing guidance documents. These models help advance potential drug candidates safely and quickly toward registration with increased probability of success and minimized the cost.

Pre-clinical: M&S in preclinical studies are applied to characterize the absorption, distribution, metabolism, and excretion of the drug candidates from discovery to Investigational New Drug-enabling studies. Non-compartmental analysis (NCA), Compartmental Pharmacokinetics (PK), and Physiologically based PK (PBPK) models can be applied to predict the disposition of drugs and characterizing PK in pre-clinical species whereas PK-PD models characterize exposure-response in these species for target identification and validation. Furthermore, these models can be applied to optimize formulation changes, possible food effects, drug-drug interaction (DDI), in addition to dose selection for clinical studies including extrapolation from animals to human dosing based on preclinical data.

Phase I: Simulation-based predictions can serve as a valuable resource when designing and optimizing clinical studies. In Phase I, M&S can support formulation changes, assess food effects and the DDI potential of drug candidates as well as guide dose escalation during ascending-dose studies. Models based on adult population data can be useful in predicting safe and efficacious doses in pediatric populations.

Phase II: In Phase II, model-based predictions can be utilized to establish proof of concept by characterizing exposure-response relationships and can serve as an indispensable tool for selecting the optimal study design, guiding the right doses and dose regimens.

Phase III: As studies progress into Phase III, these modeling tools can guide optimal sampling, analyze sparse data, and can be utilized to assess the effects of potential covariates to predict the sources of variability on the pharmacokinetics of the drug.

Furthermore, they can be employed to predict exposure in special populations (e.g., elderly, obese, pregnant, pediatric [to support the pediatric investigational plan required by EMA, and pediatric study plan required by FDA]), as well as in disease conditions providing valuable information that can support labeling.

The Pharmacometrics group at Synteract uses various validated approaches such as NCA, PBPK, Population PK, PKPD, meta-analysis to help streamline the drug development process with the ultimate goal of finding the right drug, right dosing scheme for the right patient at right time. Our team can also help to determine what type of model will be appropriate at different stages of your program and on how modeling can be benefit and support your studies.

Contact Synteract to learn how our modeling and simulation services can facilitate your drug development program.