XenoGesis
Preclinical DMPK & Bioanalysis

# Integrated Packages: Human PK & Dose Prediction

XenoGesis has developed a series of ADME packages which are designed to help clients answer key questions on how their drug discovery compounds behave in key areas such as absorption, clearance, distribution and oral bioavailability. The packages build sequentially to predict oral exposure in pre-clinical species and ultimately the likely efficacious pharmacokinetics and dose in man.

They are designed to be part of a robust iterative screening cascade during drug discovery ultimately leading to better informed decisions with an understanding of drug exposure with respect to efficacy and safety.

To find out more, contact a member of the XenoGesis team.
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This service package has been designed to predict a dosage regime in man. It uses an FDA approved PBPK modelling system, GastroPlus™ to predict human oral bioavailability, clearance and distribution. Through its validated laboratory-based assays XenoGesis will generate the data to populate the model, ensuring accurate and robust inputs which are essential to produce an accurate modelled output.

## Description of Service

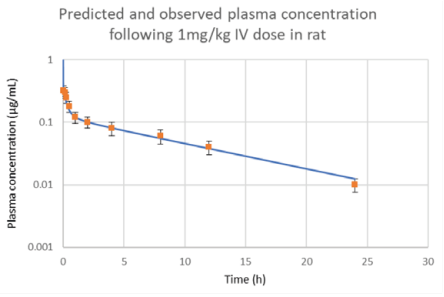
Integration of pre-clinical *in vitro* and *in vivo* data to generate a PBPK model using GastroPlus™ and use of this model to predict human PK and efficacious dose.

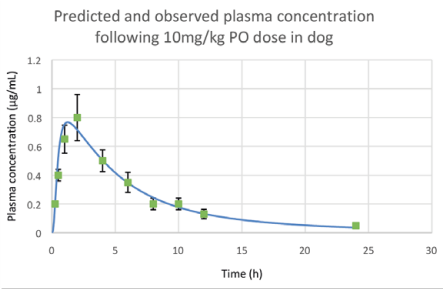
## Data collected

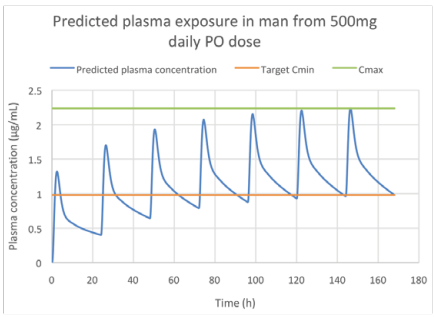
- Caco-2 permeability
- Solubility in buffer and biorelevant media (thermodynamic - ideally PBS @ pH6.5, FeSSIF, FaSSIF and SGF)
- $LogD_{7.4}$
- pKa
- Blood:plasma ratio, hepatocyte $CL_{int}$, and plasma protein binding (rat, dog and human)
- Rat and dog IV and PO PK including assessment of renal clearance

## Report format

XenoGesis will provide a written report describing the *in vitro-in vivo* correlations of absorption, clearance and distribution in rat and dog using GastroPlus™. The report will evaluate whether an adjustment of the PBPK model is required to best match the observed data (IV and PO) in these species. After such an adjustment the final GastroPlus™ PBPK model detailing the behaviour of the client drug will be generated and used within human *in vitro* data to protect oral bioavailability, clearance and distribution in man. The model will be used to identify the predicted dose regime in man required to achieve a target unbound plasma concentration-time profile provided by the client (e.g. $C_{min}$ > concentration required for 90% target engagement).




**XenoGesis Ltd is an independent laboratory-based contract research organisation specialising in pre-clinical drug metabolism & pharmacokinetics (DMPK), quantitative bioanalysis, pharmacology and expert interpretation.**

XenoGesis has state-of-the-art *in vitro*, *in vivo* and bioanalytical capabilities. With its expert pharmacokinetic/pharmacodynamic (PK/PD) interpretation and consultancy services, XenoGesis provides bespoke, iterative, data-driven feedback to clients with next step recommendations.