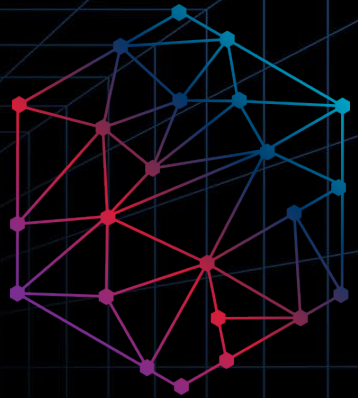
Model-Informed Drug Development

MIDD+

2021 Virtual Conference



HTPK

A bridge to Early Development

SimulationsPlus

Cognigen | DILIsym Services | Lixoft

High-Throughput PK - Vision

- Develop a simplified early PK assessment tool for non DMPK experts
- Provide dose and time-dependent modeling capabilities
- Avoid the need to input experimental values but allow their use if available
- Identify potential development issues as early as possible, even before compounds are synthesized

Partnered R&D Project

Apr 7, 2020 | Press Release

Simulations Plus Partners with Large Pharmaceutical Company to Enhance High-Throughput PBPK Capabilities in ADMET Predictor®

Keywords: ADMET cheminformatics, drug discovery, HTPK simulation module, PBPK modeling Software: ADMET Predictor® Division: Simulations Plus

Simulations Plus, Inc. (Nasdaq: SLP), the leading provider of modeling
solutions for the pharmaceutical, biotechnology, chemicals, and consu
today announced that it has entered into a new collaboration agreemer
pharmaceutical company to advance its ADMET Predictor® machine l
use within integrated drug discovery workflows. With the drugmaker's i
will develop enhanced capabilities in its existing HTPK Simulation Mod
incorporate physiologically based pharmacokinetic (PBPK) modeling in
discovery platform to support compound screening activities.

Sep 29, 2020 | Press Release

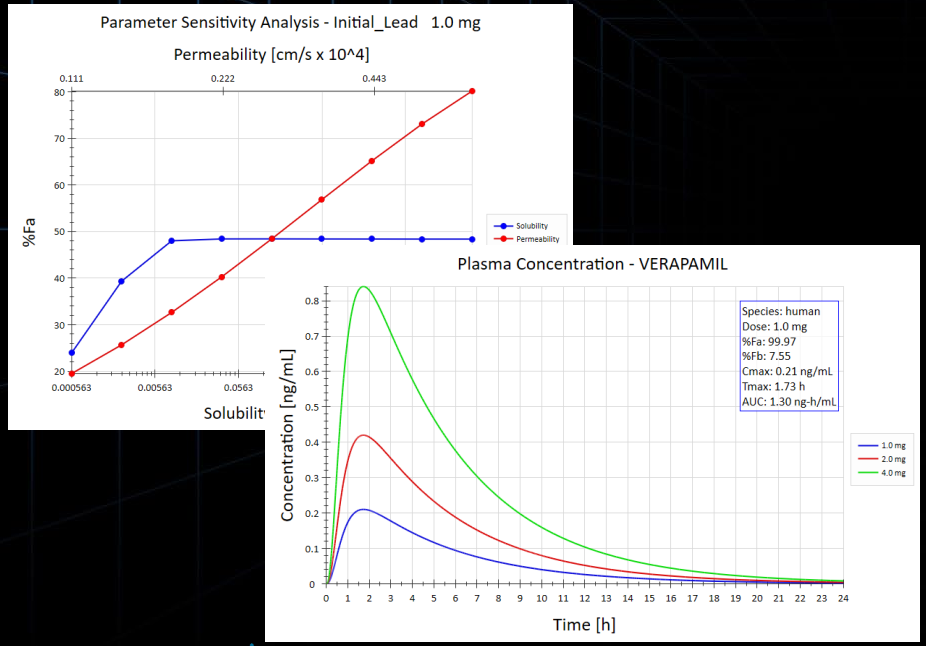
Simulations Plus Extends Partnership with Large Pharmaceutical Company to Further Expand High-Throughput PBPK Capabilities in ADMET Predictor®

Keywords: admet predictor, APX, biopharmaceutical, cheminformatics, collaboration, HTPK simulation module, pharmaceutical Software: ADMET Predictor® Division: Simulations Plus

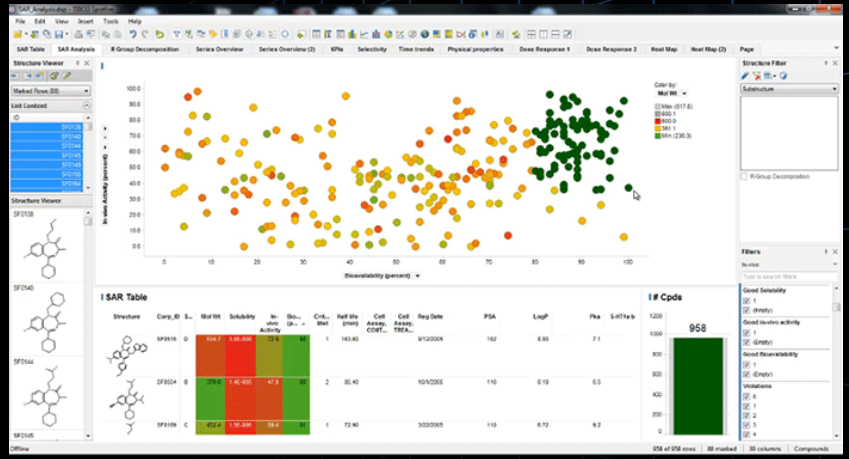
Simulations Plus, Inc. (Nasdaq: SLP), the leading provider of modeling and simulation solutions for the pharmaceutical, biotechnology, chemicals, and consumer goods industries, today announced that it has entered into an accelerated second phase of its collaboration with a large pharmaceutical company to tailor its high-throughput pharmacokinetic (HTPK) simulation functionality within ADMET Predictor® to support the sponsor partner's lead selection activities for small molecule programs.

HTPK Visualization

Native ADMET Predictor®



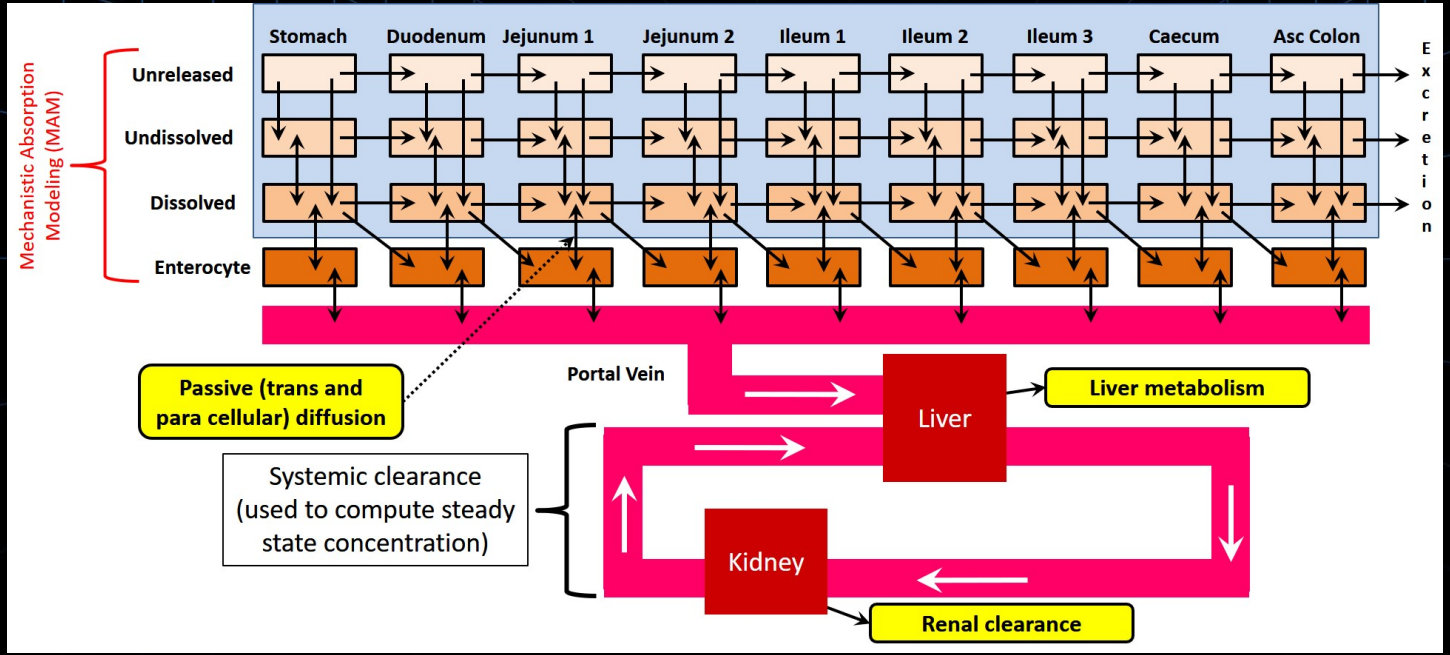
Alternate Front End



- Command-line access (Windows + Linux)
- Workflow platforms
  - Pipeline Pilot
  - KNIME

HTPK Simulation Model

ACAT™ Model* + Compartmental Model

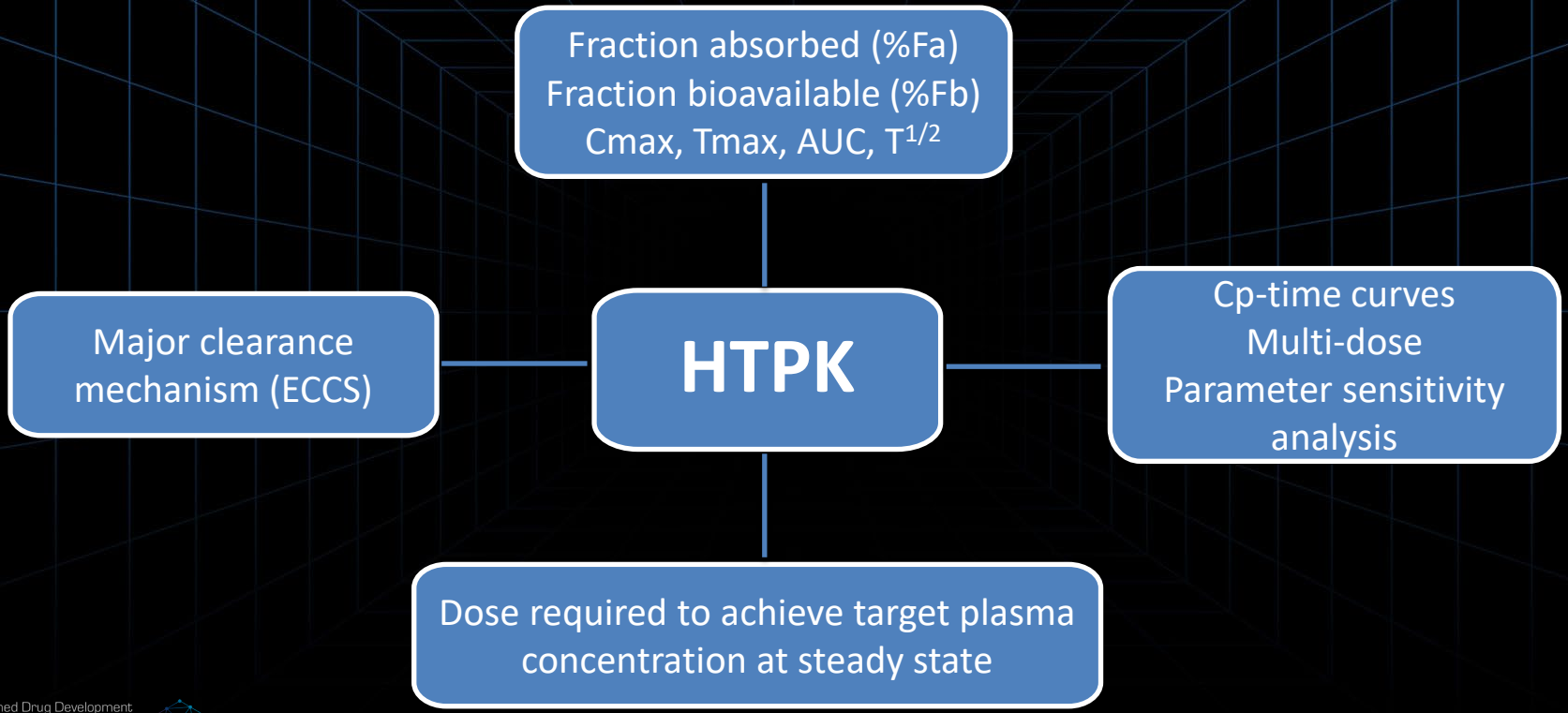


*
Advanced
Compartmental
Absorption and
Transit Model

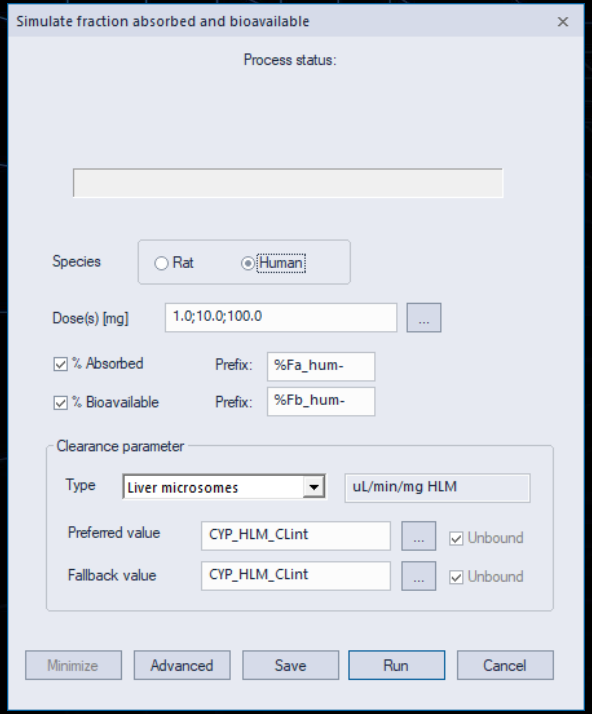
HTPK Simplifications

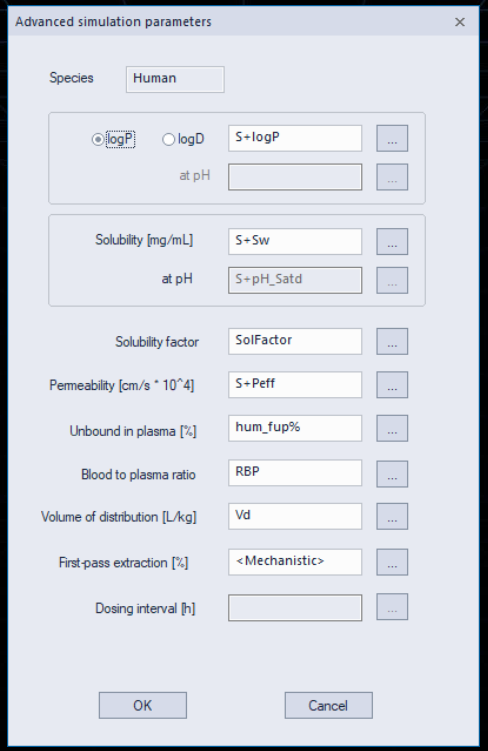
- Gut clearance is not considered
- Passive absorption kinetics only (paracellular included)
- Clearance is assumed to follow linear kinetics
- Enterohepatic circulation and biliary excretion not considered
- First-order precipitation kinetics assumed
- Dosage form is IR tablet – IV Bolus in next release
- Physiology limited to fasted adult human or rat

HTPK Predictions (APX)



HTPK Input Parameters



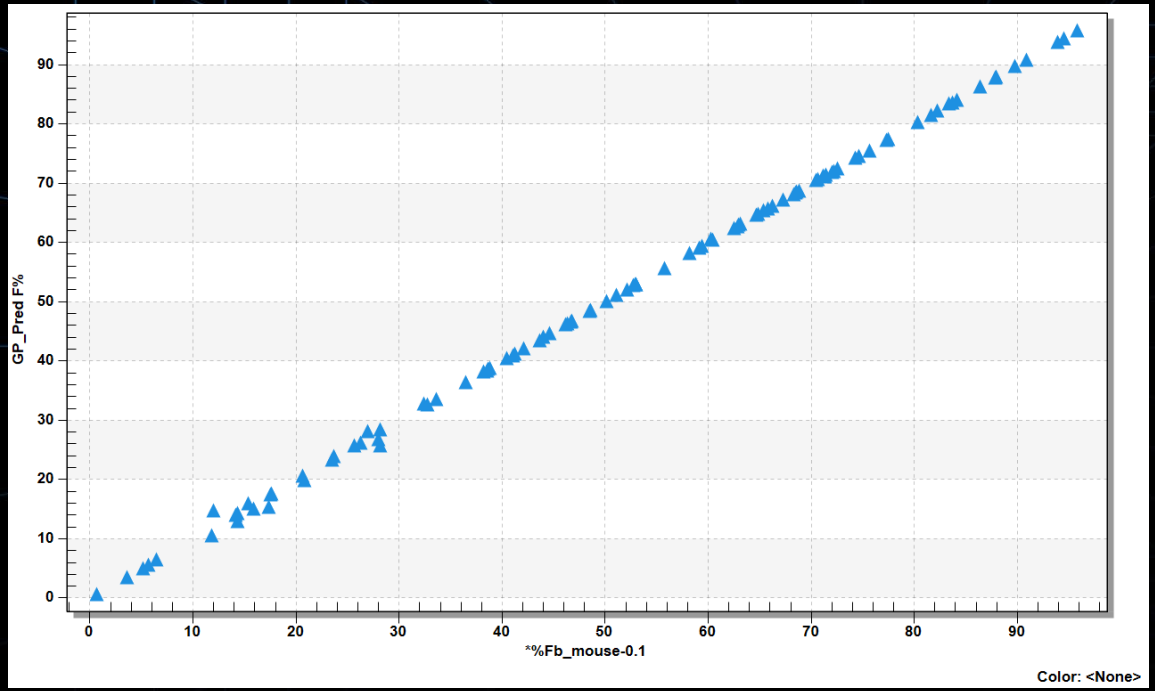


Inputs can be experimental values or predictions

Predicted inputs can be from ADMET Predictor or your own models

Configuration files contain additional parameters (e.g., particle size)

Comparison with GastroPlus®



100 compounds
Approved drugs

Time in GP
A few min…

Time in AP
…Under a sec

HTPK Performance

- Calculation of %Fa and %Fb in human after 24h.

Three different dose levels:

- 1 mg
- 10 mg
- 100 mg

10,560 diverse compounds from Enamine Diversity Set

- AP 9.5: 7min. 31 sec (23 cmpds/sec)
- APX with multithreading (7 threads): 1min 30 sec (117 cmpds/sec)

DELL Vostro Laptop - Intel® Core™ i7-8550U CPU 1.80 GHz
4 Cores, 8 Logical Processors - 16 GB RAM, Windows 10 64-bit

R&D Horizon

Spring 2021

HTPK Enhancements

- IV Bolus route of administration
- Ability to define non-specific binding
- Ability to define “free” target concentration
- Support use of Ctrough/Cmax in dose optimization
- Enhancements in command line support using .inp and .hia files

HTPK Webinar

Mark your Calendars: April 7th, 2021 at 8:00am PST

Early assessment of PK properties with the ADMET Predictor® HTPK Simulation module, a high-throughput mechanistic PBPK approach

Speaker: ?

Q&A

Questions & Answers

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Thank you for your time and attention !

Learn More! www.simulations-plus.com

SimulationsPlus

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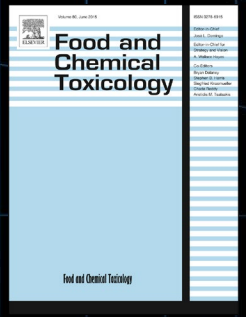
HTPK Recent Citations



Vol 140, June 2020

Liver toxicity of anthraquinones: A combined *in vitro* cytotoxicity and *in silico* reverse dosimetry evaluation

Yitong Liu, Mapa S.T. Mapa, Robert L. Sprando

Division of Toxicology, Office of Applied Research and Safety Assessment, Center for Food Safety and Applied Nutrition, U.S. Food and Drug Administration