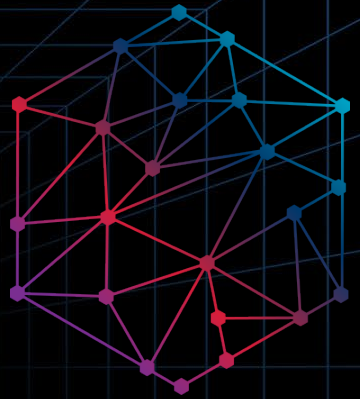
Model-Informed Drug Development

MIDD+

2021 Virtual Conference



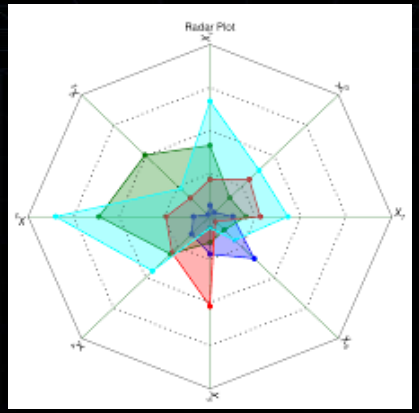
Collaborative R&D Models to Drive Innovation

SimulationsPlus

Cognigen | DILIsym Services | Lixoft

Diversity in Collaborative Formats

Value:
Cashless
$XX,XXX - $XXX,XXX



Customer:
Commercial
Government
Not-for-profit
Academic

Industry:
Pharma
Agro-chemical
Chemical

Stage:
Discovery application
Pharma development

Type of Project:
Focused SW development
New model development

Brief History of Time in Collaborations (PR)

PR Date	Subject Matter	Sponsor Institution
Jan. 12, 2021	Lung exposure model for pulmonary infections	Undisclosed
Jan. 5, 2021	Enhanced models for enhanced absorption of peptides	Undisclosed
Oct. 13, 2020	New models for oral cavity route of administration*	FDA
Sep. 29, 2020	Extension of HTPK capabilities in ADMET Predictor® (II)	Large pharma
Sep. 22, 2020	Validation of AI-driven drug design capabilities	Large pharma
May 28, 2020	Interspecies translation for ocular drug delivery (3 yr)	FDA
Apr. 7, 2020	Extension of HTPK capabilities in ADMET Predictor® (I)	Large pharma
Feb. 4, 2020	QSP model development for heart failure	Large pharma
Dec. 5, 2019	Extension to structure and tautomer handling	Bayer AG

* With St. Louis college of Pharmacy

Non Press Released

Date	Subject Matter	Sponsor Institution
Jun. 2020	Provide capabilities for building site of metabolism models for alternate species	Agrochemical company

- ➔ Provide software with capabilities similar to in-house development version
- ➔ Provide access to proprietary atom-based descriptors
- ➔ Provide technical assistance with implementation
- ➔ Provide scientific support for use in SOM model development

ADMET Predictor® AIDD Technology

Sep 22, 2020 | Press Release

Simulations Plus Partners with Large Pharmaceutical Company to Validate AI-Driven Drug Design Capabilities in ADMET Predictor®

Keywords: admet predictor, AIDD, antimalarial design study, collaborative research agreement Software: ADMET Predictor® Division: Simulations Plus

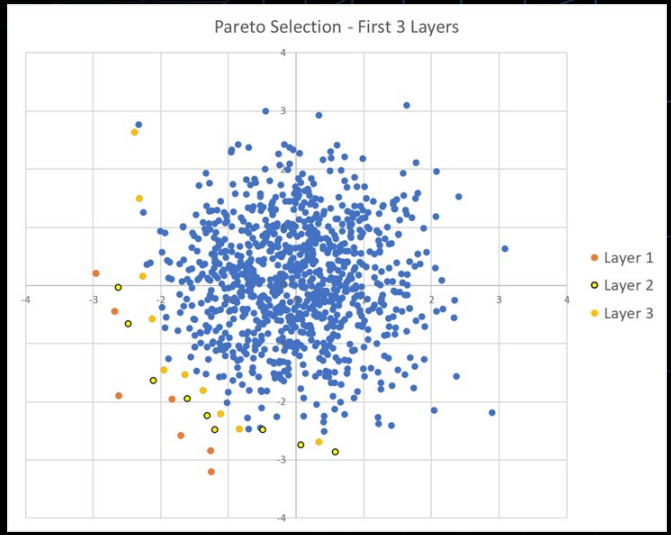
Simulations Plus, Inc. (Nasdaq: SLP), the leading provider of modeling and simulation solutions for the pharmaceutical, biotechnology, chemicals, and consumer goods industries, today announced that it entered into a collaborative research agreement with a large pharmaceutical company to evaluate the new AIDD Module in the recently launched version of ADMET Predictor®.

Very active space with new companies

ADMET Predictor® AIDD Technology

New Technology release with APX in Sep. 2020:

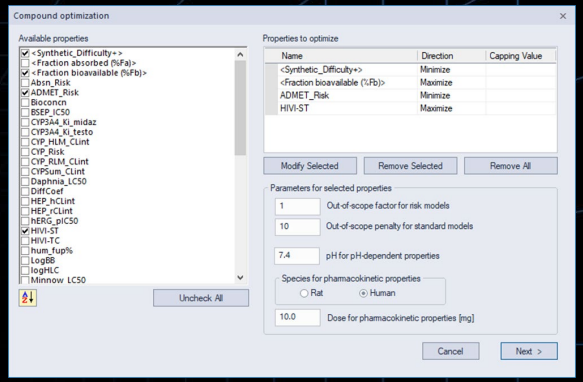
- Generative chemistry engine with chemically intelligent transforms
- Highly customizable
- Fast property calculations (including mechanistic PK)
- Pareto-based selection process
- Smart and customizable MedChem filters

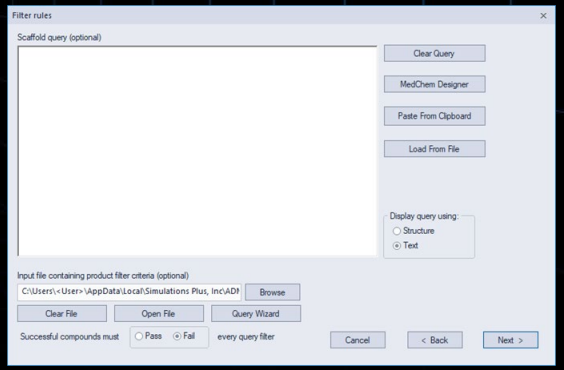


ADMET Predictor® AIDD Technology

Motivation: Answer some key questions

- How does it operate in a real pharma research environment?
- Can it adapt to project specifics?
- Can it keep-up with MedChem team requirements?
- How does it change the CompChem vs MedChem dynamics?
- How much human input is required?
- Did we improve the compounds?





ADMET Predictor® HTPK Simulation

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.

ADMET Predictor® HTPK Simulation

Phase I

- Enhancements in command line support using .inp and .hia files
- New C_{ave} definition as AUC/Dose
- Output multiple Cp time curves
- Multi-dosing
- Extended output options for AUC, C_{max} and T_{max}

Phase II

- IV Bolus route of administration
- Ability to define non-specific binding
- Ability to define “free” target concentration
- Support use of $C_{trough/Cmax}$ in dose optimization

ADMET Predictor® HTPK Simulation

Timeline:

- Phase I: Jan. 2020 – Jun. 2020
  - ➔ Commercial software release Sep. 16, 2020

- Phase II: Sep. 2020 – Feb. 2021
  - ➔ Commercial software release Apr./May 2021

pKa Model Development with Bayer AG

Timeline: April 2012

JOURNAL OF CHEMICAL INFORMATION AND MODELING

Article

pubs.acs.org/jcim

Best of Both Worlds: Combining Pharma Data and State of the Art Modeling Technology To Improve *in Silico* pK_a Prediction

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pKa Model Development

Problem Statement:

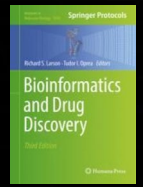
Public datasets for pKa data are limited to ca. 10,000 compounds w/ ca 14,000 pKa values

Large pharma companies have extensive amounts of data

➔ Expansion of chemical space

Large amount of data curation typically required on public data sources

➔ High LOE for model development*



Building a Quantitative Structure-Property Relationship (QSPR) Model

Bioinformatics and Drug Discovery pp 139-159 | Cite as

- Robert D. Clark (1) Email author (bob@simulations-plus.com)
- Pankaj R. Daga (1)

pKa Model Development

Problem Statement:

Data from pharma companies is highly confidential. We need to guarantee:

➔ Confidentiality of the data

➔ No ability to reverse-engineer in the software

Large pharma have extensive tools and competencies so the bar is high

➔ Show originality and added value

…at the end of day, it worked!

pKa Model Development

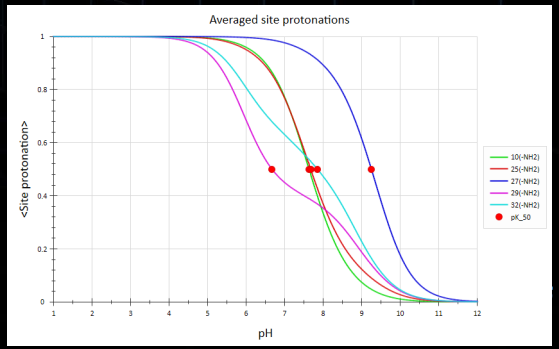
Solution Statement:

Joint development leading to:

- ➔ 19,464 multiprotic ionization macroconstants from Bayer alone
- ➔ 14,176 multiprotic ionization macroconstants from public sources

➔ Total of 33,640 values (over 2x what is available from public sources)

- ➔ Most accurate commercially available pKa model
- ➔ Powerful implementation in ADMET Predictor®
- ➔ Key effect of ionization on other properties



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Focused R&D vs Consortium Development

Focused R&D Collaboration

- Typically short timeline (3-9 months)
- Financial commitment $$
- Contractual deliverables
- 1-on-1 communication with client

Consortium R&D

- Multi-year commitment
- Financial commitment $$$$
- Final deliverables based on other members votes
- Consortium meetings

Areas of Active Exploration

Data, data, data…

ChemInformatics

- Tautomer-independent models
- Automated data curation
- AI technology

Models

- Solubility
- Plasma Protein Binding
- Transporters
- Microsomal stability
- CYP Inhibition / Induction
- Intestinal permeability
- UGT metabolism

Q&A

Questions & Answers

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Learn More! www.simulations-plus.com

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