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The "Leaves" of the OSP Suite

OPEN SYSTEMS PHARMACOLOGY

Outline

- Vision and Mission of the OSP
- The OSP Community Landscape
  - OSP MT, Focus Groups and Users
- Intra- & Extra-Community Collaboration
- Sprouting Leaves
- Food for Thought

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Vision and Mission of the OSP

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Vision and Mission of the OSP

https://github.com/Open-Systems-Pharmacology/Roadmap

Robust and reliable, easy-to-use modeling & simulation tools, processes and models for pharmaceutical and other life-sciences applications qualified and accepted by a scientific community from academia, regulatory agencies and industry available and open to everyone.

Provide a platform for joint development, review & qualification, and application of state-of-the-art tools for PBPK and Systems Pharmacology modeling and an open library of models for application as well as method & tool qualification purposes. Promote the idea of pre-competitive open collaboration for the advancement of modeling & simulation sciences in pharmaceutical and life science.

The OSP Community Landscape

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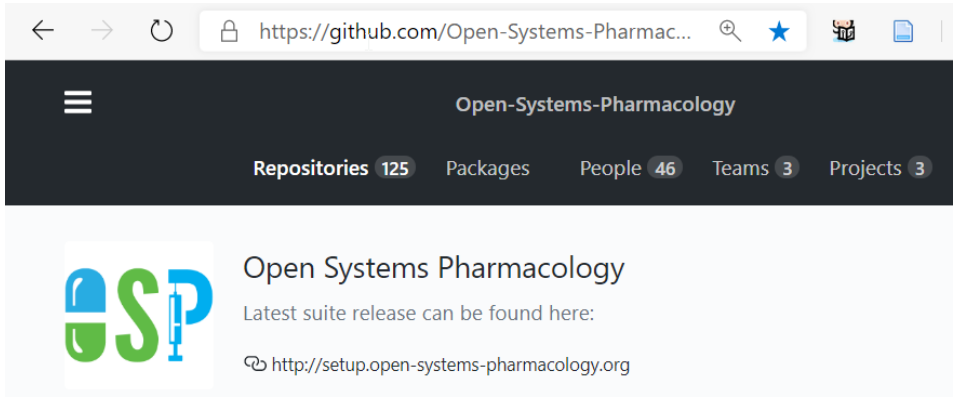
OSP OPEN SYSTEMS PHARMACOLOGY

The OSP Community Landscape

Stakeholders of the **Open Systems Pharmacology** community and **Management Team**



Open Source since 2017 on GitHub

MANAGEMENT TEAM

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Design2Code Inc.

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Systems Pharmacology & Medicine, Bayer AG

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esqlabs
we empower life sciences

SANOFI

BAYER

NOVARTIS

Boehringer Ingelheim

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RWTH AACHEN UNIVERSITY

Pharmetheus
Pharmacometrics Consulting Services

The OSP Community Landscape

Stakeholders of the **Open Systems Pharmacology** community and **Management Team**

Dedicated Focus Groups have been established to conceptualize, design and progress the individual areas, the Management Team will coordinate the interplay of focus areas and interfaces between them

Focus groups shall be the owner of the development in the respective focus area, they are expected to conceptualize and coordinate activities of the respective field.

- DDI
- Special Populations
- Absorption
- PD
- Statistical modelling
- First in Human (IVIVE)
- Omics
- Suite Release Management
- Automation/Qualification
- Community Engagement (PR)
- Biologics
- Nonclinical PBPK
- PBBM
- HT PBPK

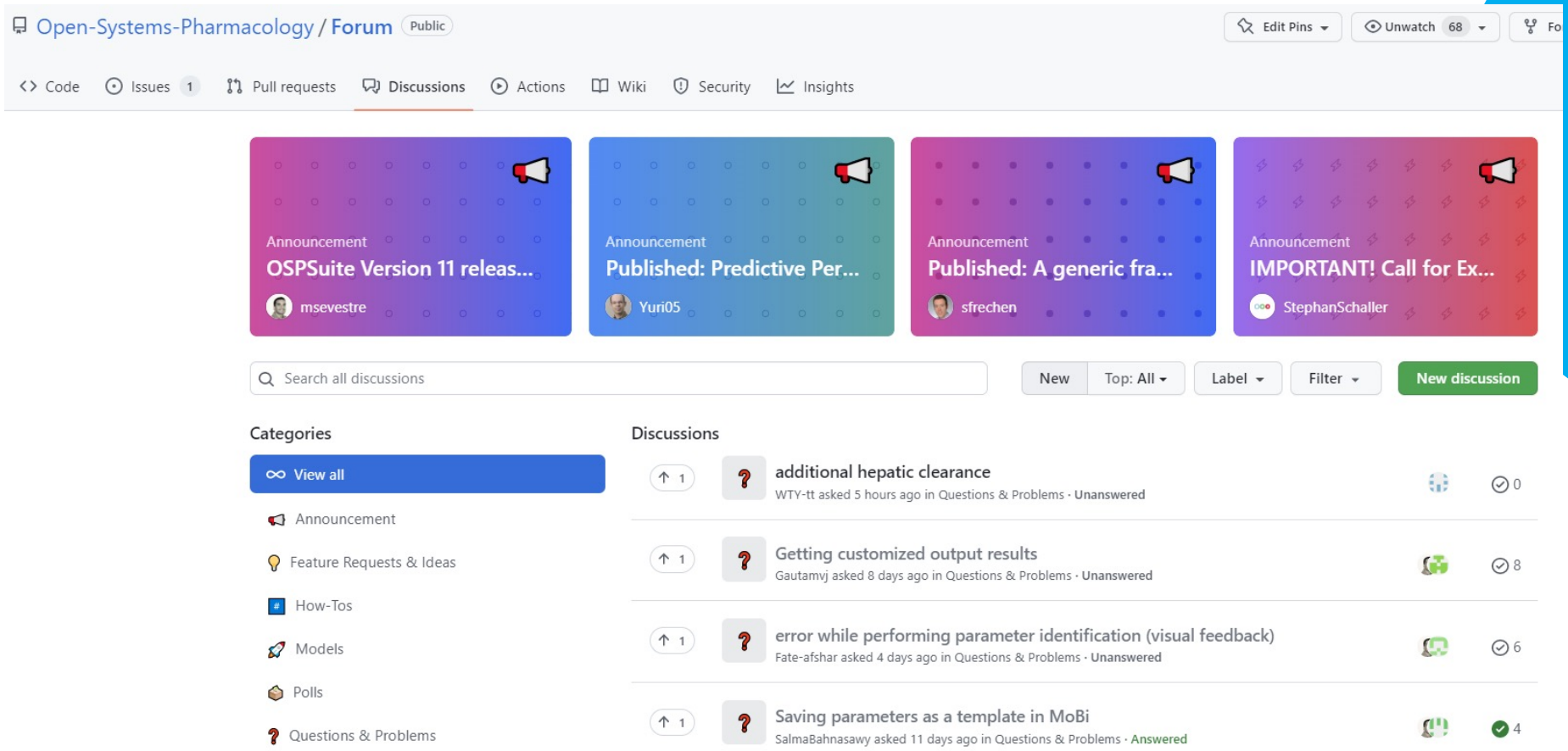
DDI	Quantitative DDI predictions (CYPs as well as transporters) are one of the key applications for PBPK and are a prerequisite for designing efficient clinical development programs and studies. A comprehensive library of well documented, qualified perpetrators and victims is a prerequisite for acceptance of DDI predictions from regulatory authorities.	Sebastian Frechen (@sfrechen)
IVIVE	• Improve and facilitate use of IVIVE in PK-Sim • Provide guidelines on how to conduct IVIVE in PK-Sim • Facilitate integration of in vitro data in prediction of DDI (e.g. integration of fraction metabolized) • Extrapolation of Caco-2 permeabilities to effective permeabilities	Donato Teutonico (@teutonicod)
Special populations	The addition of new or updated virtual populations is required to expand the application scope of the software in a consistent manner across users. The overall objectives are to define a process for 1. technical generation of populations destined for the OSP Suite and, 2. evaluation of those populations. This protocol will allow populations to be added more efficiently.	Andrea Edginton (@Aedginto)
Statistical Modelling	Statistical Modeling is a strategic theme of the OSP MT. Statistical modeling is a key enabler for PBPK and QSP M&S. Respective capabilities are required for all application areas to quantitatively	Christian Diedrich (@DiedrichC)

The OSP Community Landscape

User Community: Forum: github.com/Open-Systems-Pharmacology/Forum

FORUM

Have your questions answered or provide answers to others. The Forum is a great way to stay up-to-date on the community buzz around OSP.



Community Collaboration(s)

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Community Collaboration(s)

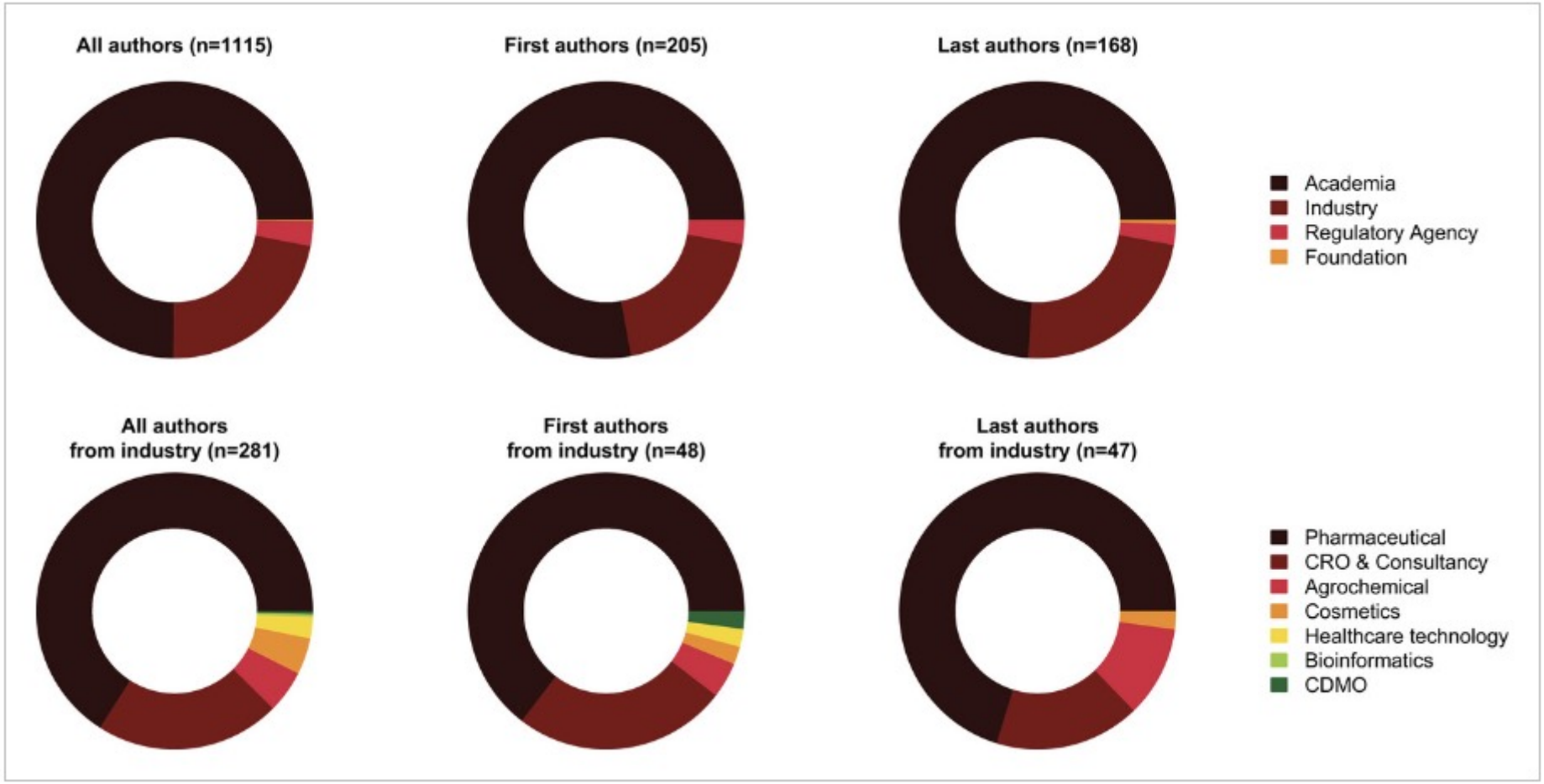
The Journal of Clinical Pharmacology
Official Publication of the American College of Clinical Pharmacology

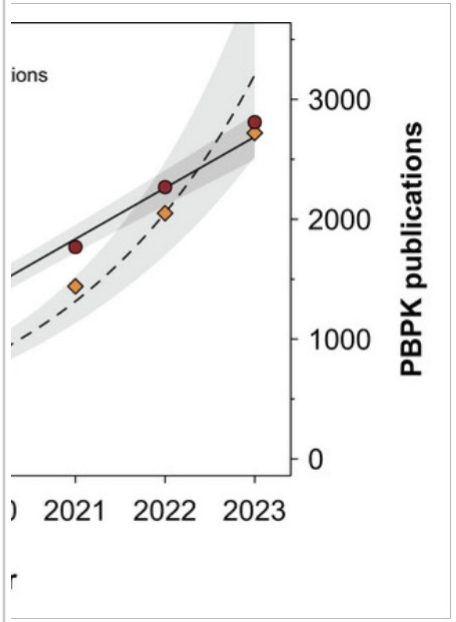
Editor's Choice: Original Article | Open Access

In-Depth Analysis of the Selection of PBPK Modeling Tools: Bibliometric and Social Network Analysis of the Open Systems Pharmacology Community

André Dallmann PhD, Donato Teutonico PhD, Stephan Schaller PhD, Rolf Burghaus PhD, Sebastian Frechen MD

Community Collaboration(s)





Community Collaboration(s)

Let's FILL this Space

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"Sprouting Leaves"

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Sprouting Leaves

Chemicals & Pharmaceuticals

Software development

Route and organism specific toxicokinetics simulations

Structure – toxico/pharmacokinetics simulations & read-across

***In vivo* toxicity and adverse outcome modeling**

Formulation design and bioequivalence simulations

Drug dosing - pharmacokinetic and pharmacodynamic simulations

***In silico* assessment of drug-drug interaction**

Model-based translation between populations

Disease, drug effect and trial modeling

Sprouting Leaves

Chemical Risk Assessment

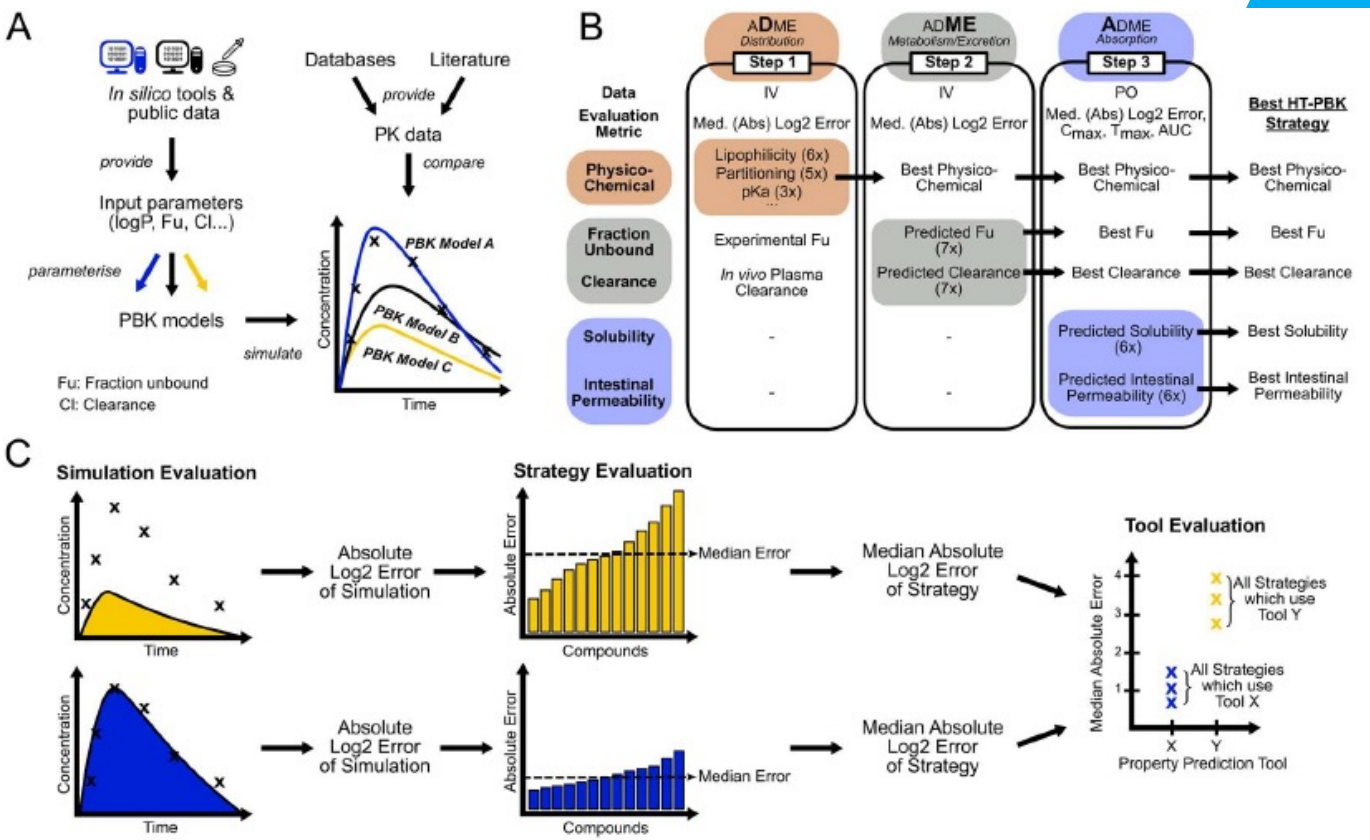
Archives of Toxicology
https://doi.org/10.1007/s00204-024-03764-9

IN SILICO

Systematic evaluation of high-throughput PBK modelling strategies for the prediction of intravenous and oral pharmacokinetics in humans

René Geci[1,2] · Domenico Gadaleta[3] · Marina García de Lomana[4] · Rita Ortega-Vallbona[5] · Erika Colom Eva Serrano-Candelas[5] · Alicia Paini[1] · Lars Kuepfer[2] · Stephan Schaller[1]

- PBK simulations for more than 200 chemicals for IV and oral exposure scenarios in humans and compared to *in vivo* data in the literature.
- Systematically tested different parameterization strategies.

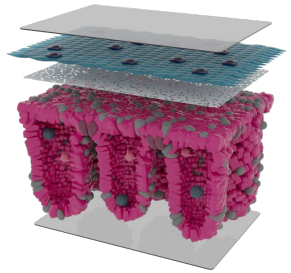


Sprouting Leaves
(Q)IVIVE

In Vitro	In Silico	In Vivo

e.g. Organ-on-Chip

Industry



OoC Information

Experimental Design

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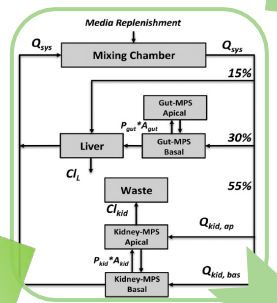
Drug Information

Unknown Pharmacology

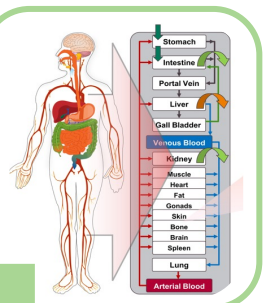
Data

OoC-PBK



Computational Model Development

Human PBK



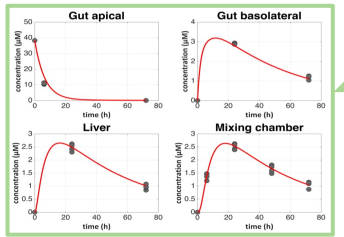
Measured, OoC-specific…

…Drug PK/PD
Efficacy Safety
ADME

…Biomarkers
ALT Tumor growth
Cytokines Urea

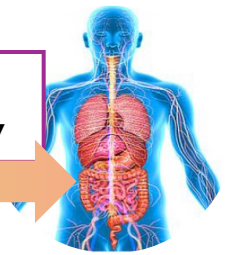
Input

Analysis



Input

Prediction human Pharmacology



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“Food for Thought”

How to Continue from here

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Regulatory Submissions with PK-Sim

OSP file formats are added to FDA's white list of file formats for electronic submissions

The following OSP file formats are included:

- **.pksim5** (PK-Sim project file)
- **.mbp3** (MoBi project file)
- **.pkml** (OSP model exchange format)
- **.json** (PK-Sim project snapshots file)

Specifications for File Format Types Using eCTD Specifications

Revision History

Date	Version	Summary of Changes
2023-12-01	9.0	Updated .docx permissible uses Updated .xml accepted locations and permissible uses Removed "CDER Only" from permissible uses for: .csv, .cas, .dat, .rmd, .r Updated file format added: Modeling & Simulation file types: .pksim5, .mbp3, .pkml, .json, .mlxtran, .mlxproperties, .pkx, .pkxproperties, smlx, .smlxproperties, .syc, .datxplore

https://www.fda.gov/media/85816/download

Food for Thought

Think about what you learn

→ Think about what you are still missing (Free Feedback)