

# Tools and workflows for automated reporting of PBPK modeling with OSP

Felix Mil (ESQlabs GmbH)

Ghazal Montaseri (Boehringer Ingelheim Pharma GmbH & Co. KG)

September 30, 2025 | OSP Community Conference | Paris

*Life forward*

# PBPK Automated Reporting: Why, what and how

## Why:

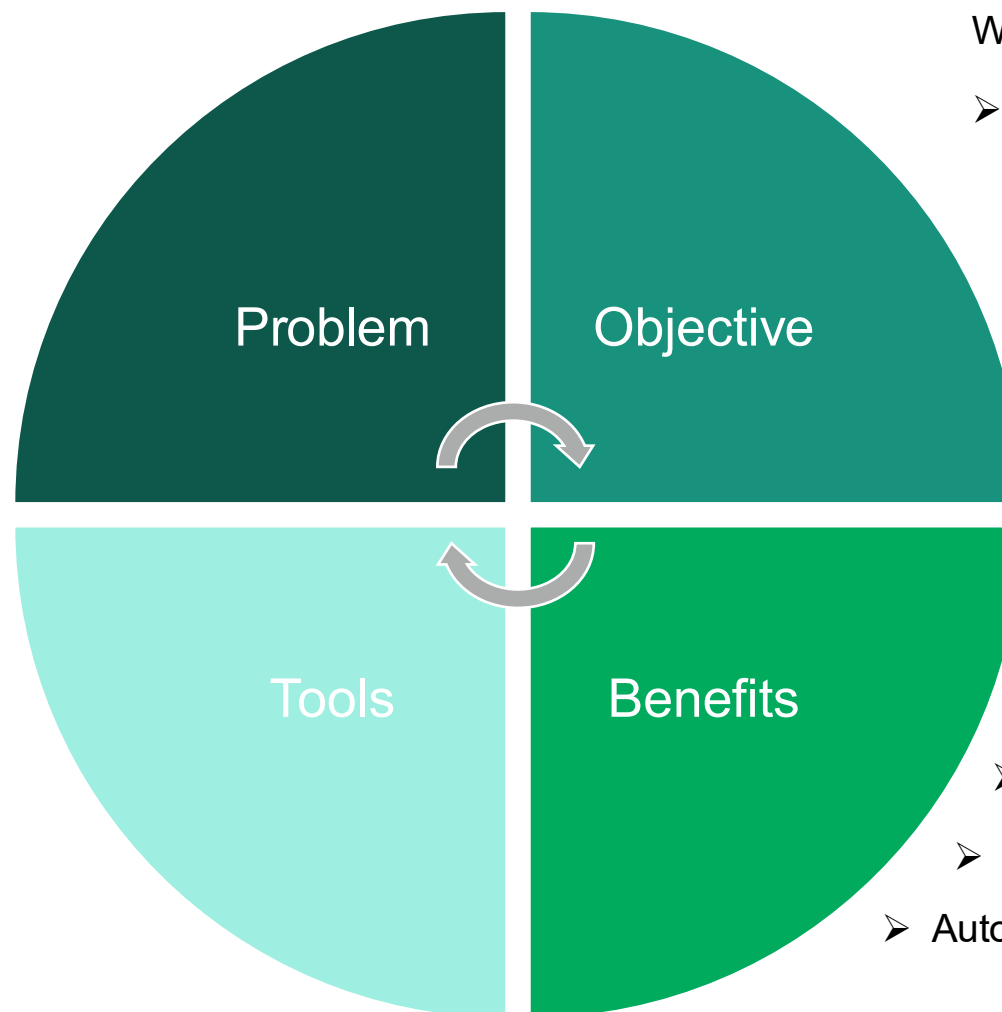
- Reporting PBPK analysis results is typically done **manually** by copying/inserting relevant tables and figures into a Word document or a LaTeX template.
- This process is inefficient, time-consuming, and prone to errors.

## How:

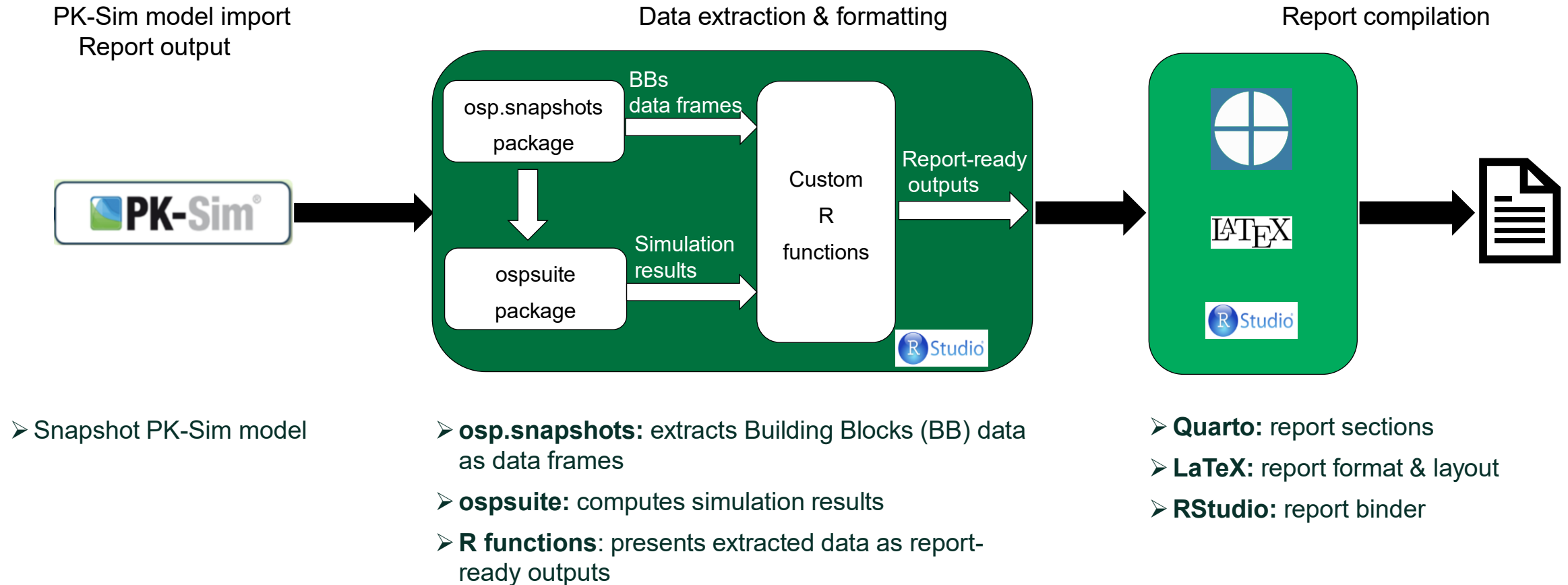
- Rstudio & OSPS R packages
  - osp.snapshots package
  - ospsuite package

## What:

- Within **Boehringer Ingelheim**, automation techniques were implemented to **enhance the efficiency** of PBPK report generation.
- Faster reporting
- Consistent quality
- Fewer manual errors
- Simplified QC process
- Auto-generated figures and tables



# Automated PK-Sim®-Related Reporting Workflow at Boehringer Ingelheim



# osp.snapshots Package: from Compounds BB Input to Output

Input: snapshot data/nested object

intermediate: osp.snapshots data frame

Output:  
customized table

```
"Compounds": [
  {
    "Name": "ExampleDrug",
    "IsSmallMolecule": true,
    "PlasmaProteinBindingPartner": "Albumin",
    "Lipophilicity": [...],
    "FractionUnbound": [...],
    "Solubility": [...],
    "IntestinalPermeability": [...],
    ...
  }
]
```

compound	category	type	parameter	value	unit	data_source	source
ExampleDrug	physicochemical_property	lipophilicity	Optimized	2.8972038771	Log Units	NA	Parameter optimization
ExampleDrug	physicochemical_property	fraction_unbound	Gertz et al. 2010	0.031	NA	NA	Parameter optimization
ExampleDrug	physicochemical_property	molecular_weight	NA	325.78	g/mol	NA	Hu et al., 2005
ExampleDrug	physicochemical_property	halogens	Cl	1	NA	NA	Hu et al., 2005
ExampleDrug	physicochemical_property	halogens	F	1	NA	NA	Hu et al., 2005
ExampleDrug	physicochemical_property	pKa	base	6.2	-	-	Wang et al., 2024
ExampleDrug	physicochemical_property	pKa	acid	10.95	-	-	Wang et al., 2024
ExampleDrug	physicochemical_property	solubility	pH 6.5	0.049	mg/mL	-	mann et al., 2005
ExampleDrug	physicochemical_property	intestinal_permeability	Optimized	0.049	cm/min	-	Parameter optimization
ExampleDrug	protein_binding_partners	SpecificBinding	koff, GABRG2	1	1/min	-	Parameter optimization
ExampleDrug	protein_binding_partners	SpecificBinding	Kd, GABRG2	1.8	nmol/L	-	Calculated
ExampleDrug	metabolizing_enzymes	MetabolizationLiverMicrosomes_MM	Km, CYP3A4	4	µmol/L	-	Zwald et al., 2001
ExampleDrug	metabolizing_enzymes	MetabolizationLiverMicrosomes_MM	kcat, CYP3A4	8.761	1/min	-	Parameter optimization
ExampleDrug	metabolizing_enzymes	MetabolizationLiverMicrosomes_MM	Km, UGT1A4	37.8	µmol/L	-	Zwald et al., 2001
ExampleDrug	metabolizing_enzymes	MetabolizationLiverMicrosomes_MM	kcat, UGT1A4	4.759	1/min	-	Zwald et al., 2001
ExampleDrug	renal_clearance	GlomerularFiltration	GFR fraction	0.6401	-	-	Parameter optimization

Parameter	Value	Unit	Source
Lipophilicity	2.897	Log Units	Parameter optimization
Fu-plasma	0.031	-	Parameter optimization
Molecular Weight	325.8	g/mol	Hu et al., 2005
Halogens, Cl	1	-	Hu et al., 2005
Halogens, F	1	-	Hu et al., 2005
pKa, base	6.2	-	Wang et al., 2024
pKa, acid	10.95	-	Wang et al., 2024
Solubility, pH 6.5	0.049	mg/mL	mann et al., 2005
Intestinal transcellular permeability	1.555e-04	cm/min	Parameter optimization
koff, GABRG2	1	1/min	Parameter optimization
Kd, GABRG2	1.8	nmol/L	Calculated
Km, CYP3A4	4	µmol/L	Zwald et al., 2001
kcat, CYP3A4	8.761	1/min	Parameter optimization
Km, UGT1A4	37.8	µmol/L	Zwald et al., 2001
kcat, UGT1A4	4.759	1/min	Zwald et al., 2001
GFR fraction	0.6401	-	Parameter optimization

☒ Is small molecule

Lipophilicity:

Experiment

Lipophilicity

Value Origin

Optimized

2.8972 Log Units

Parameter Identification-Par...

Fraction unbound (plasma, reference value):

Binds to:

Albumin

α1-acid glycoprotein

Unknown

Experiment

Fraction Unbound

Species

Value Origin

Gertz et al. 2010

0.0310

Human

Parameter Identific...

Molweight:

Molecular weight

325.7800 g/mol

Has halogens

Yes

Effective molecular weight

286.7800 g/mol

Value origin

Publication-Hu et al., 2005

Compound type / pKa:

Base

6.2000

Acid

10.9500

Neutral

<None>

Value origin

Publication-Wang et al., 2024

Solubility:

Experiment

Solubility at Re...

Ref-pH

Solubility gain p...

pH-dependent

Value Origin

PaSS3F

0.0490 mg/ml

6.5000

1000.0000

Show Graph

Publicati...



# Automated Table of Expression Profiles BB

Expression Profile: 'CYP3A4|Human|European (P-gp modified, CYP3A4 36 h)'

Species: Human

Metabolizing enzyme: CYP3A4

Phenotype: European (P-gp modified, CYP3A4 36 h)

Name	Value
Reference concentration	4.3200 µmol/L
t1/2 (liver)	36.0000 h
t1/2 (intestine)	23.0000 h

Ontogeny/variability like: CYP3A4

Expression Profile: 'OATP1B1|Human|Korean (Yu 2004 study)'

Species: Human

Transport protein: OATP1B

Phenotype: Korean (Yu 2004 study)

Name	Value
Reference concentration	1.4100 µmol/L
t1/2 (liver)	36.0000 h
t1/2 (intestine)	23.0000 h

Ontogeny/variability like: P-gp

Expression Profile: 'P-gp|Human|European (P-gp modified, CYP3A4 36 h)'

Species: Human

Transport protein: P-gp

Phenotype: European (P-gp modified, CYP3A4 36 h)

Name	Value	Value Origin
Reference concentration	1.4100 µmol/L	Publication-Riemann 2001
t1/2 (liver)	36.0000 h	Publication-Riemann 2001
t1/2 (intestine)	23.0000 h	Publication-Riemann 2001

Ontogeny/variability like: P-gp

Table of expression profiles parameters

Molecule	Phenotype	Parameter	Value	Unit	Source
<b>Metabolizing Enzymes</b>					
AADAC	European (P-gp modified, CYP3A4 36 h)	Reference concentration	1	µmol/L	Assumed
	European (P-gp modified, CYP3A4 36 h)	t1/2 (liver)	36	h	Berg et al., 2004
	European (P-gp modified, CYP3A4 36 h)	t1/2 (intestine)	23	h	Berg et al., 2004
	Korean (Yu 2004 study)	Reference concentration	1	µmol/L	PK-Sim default
	Korean (Yu 2004 study)	t1/2 (liver)	36	h	Hu et al., 2018
	Korean (Yu 2004 study)	t1/2 (intestine)	23	h	Hu et al., 2018
CYP3A4	European (P-gp modified, CYP3A4 36 h)	Reference concentration	4.32	µmol/L	Utkin 2001
	European (P-gp modified, CYP3A4 36 h)	t1/2 (liver)	36	h	Utkin 2001
	European (P-gp modified, CYP3A4 36 h)	t1/2 (intestine)	23	h	Utkin 2001
	Korean (Yu 2004 study)	Reference concentration	3.63	µmol/L	Parameter optimization
	Korean (Yu 2004 study)	t1/2 (liver)	36	h	Assumed
	Korean (Yu 2004 study)	t1/2 (intestine)	23	h	Assumed

Table of proteins, phenotypes, assays, and ontogeny

Molecule	Phenotype	Assay	Ontogeny/Variability <sup>+</sup>
<b>Metabolizing Enzymes</b>			
AADAC	European (P-gp modified, CYP3A4 36 h)	EST	No
AADAC	Korean (Yu 2004 study)	EST	No
CYP3A4	European (P-gp modified, CYP3A4 36 h)	RT-PCR	Yes
CYP3A4	Korean (Yu 2004 study)	RT-PCR	Yes
UGT1A4	European (P-gp modified, CYP3A4 36 h)	Array	Yes
<b>Protein Binding Partners</b>			
ATP1A2	European (P-gp modified, CYP3A4 36 h)	EST	No
ATP1A2	Korean (Yu 2004 study)	RT-PCR	No
GABRG2	European (P-gp modified, CYP3A4 36 h)	RT-PCR	No
GABRG2	Korean (Yu 2004 study)	RT-PCR	No
<b>Transporters</b>			
OATP1B1	European (P-gp modified, CYP3A4 36 h)	Array	No
OATP1B1	Korean (Yu 2004 study)	RT-PCR	No
P-gp	European (P-gp modified, CYP3A4 36 h)	Array	Yes

# Automated Table of Individuals and Populations BB

Individual: 'European (P-gp modified, CYP3A4 36 h)'

Biometrics

Anatomy & Physiology

Expression

Population Properties

Species: Human

Population: East Asian (Tanaka, 1996)

Gender: Male

Calculation methods: Endothelial surface areas, Organ vascularization, Body surface area, Mosteller

Individual Parameters

Age: 30.0000

Weight: 73.0000

Height: 176.0000

BMI: 23.5666

Individual: 'Korean (Yu 2004 study)'

Biometrics

Anatomy & Physiology

Expression

Population Properties

Species: Human

Population: East Asian (Tanaka, 1996)

Gender: Male

Calculation methods: Endothelial surface areas, Organ vascularization, Body surface area, Mosteller

Individual Parameters

Age: 23.3000 year(s)

Weight: 66.5839 kg

Height: 172.9000 cm

BMI: 22.2730 kg/m<sup>2</sup>

Table of individual characteristics

Individual name	Age [year(s)]	Weight [kg]	Height [cm]	BMI [kg/m <sup>2</sup> ]	Gender	Database	Expression*
European (P-gp modified, CYP3A4 36 h)	30	73.0	176	23.6	Male	European	CYP3A4/European (P-gp modified, CYP3A4 36 h), P-gp/European (P-gp modified, CYP3A4 36 h)
Korean (Yu 2004 study)	23.3	66.9	173	22.4	Male	East Asian	CYP3A4/Korean (Yu 2004 study), AADAC/Korean (Yu 2004 study), OATP1B1/Korean (Yu 2004 study), GABRG2/Korean (Yu 2004 study)

Population: 'European overweight population'

Demographics

Expression

User Defined Variability

Distribution

Population Properties

Number of individuals: 10

Proportion of females [%]: 50

Population Parameters Ranges

Age: from

Weight: from

Height: from

Population: 'European population'

Demographics

Expression

User Defined Variability

Distribution

Population Properties

Number of individuals: 100

Proportion of females [%]: 50

Population Parameters Ranges

Age: from 23.0000 to 56.0000 year(s)

Weight: from 45.0000 to 90.0000 kg

Table of population characteristics

Population name	Age [year(s)]	Weight [kg]	Height [cm]	BMI [kg/m <sup>2</sup> ]	Number of individuals	Proportion of females [%]	Based on individual
European overweight population	69.0 [19.7%]	80.1 [17.6%]	16.2 [5.39%]	30.7 [19.4%]	10	50	European (P-gp modified, CYP3A4 36 h)
	70.2 [13.8]	81.1 [14.2]	16.2 [0.871]	31.2 [6.06]			
	54.5, 90.3	70.2, 107	15.2, 17.3	24.4, 40.7			
	45-98	70-140	150-180	23.7-44.3			
European population	38.4 [24.6%]	67.8 [15.7%]	168 [7.25%]	24.1 [12.4%]	100	50	European (P-gp modified, CYP3A4 36 h)
	39.7 [9.76]	68.7 [10.8]	168 [12.2]	24.3 [3.00]			
	23.9, 53.8	52.7, 87.6	153, 189	20.9, 29.3			
	23-56	45-90	133-198	18.9-39.9			

\*The first line for each population characteristics showed geometric mean [coefficient of variation %]

The second line for each population characteristics showed mean [standard deviation]

The third line for each population characteristics showed 5th percentile, 95th percentile

The fourth line for each population characteristics showed minimum-maximum

# Automated Table of Other BB



Parameter	Value	Unit	Source
<b>Tablet (Lint80)</b>			
Dissolution time (80% dissolved)	240	min	Hu et al., 2005
Lag time	12	min	Hu et al., 2005
Use as suspension	yes	-	Hu et al., 2005
<b>Tablet (Weibull)</b>			
Dissolution time (50% dissolved)	0.0107	min	Parameter optimization
Lag time	0	min	Assumed
Dissolution shape	4.38	-	Parameter optimization
Use as suspension	yes	-	Wang et al., 2022



Parameter	Name/Value [unit]
<b>iv 0.001 mg (5 min)</b>	
<b>Scheme item 1</b>	
Application type	Intravenous
Start time	0 [h]
Dose	0.001 [mg]
Number of repetitions	1 [-]
Time Between repetitions	0 [h]
<b>Mikus 2017</b>	
<b>Scheme item 1</b>	
Application type	Intravenous
Start time	6 [h]
Dose	2 [mg]
Number of repetitions	1 [-]
Time Between repetitions	0 [h]
<b>Scheme item 2</b>	
Application type	Oral
Formulation	Tablet (Weibull)
Start time	0 [h]
Dose	4 [mg]
Number of repetitions	1 [-]
Time Between repetitions	0 [h]

# BB Data Presentation as Text Blocks

## Metabolizing Enzymes kinetics

In the final PBPK model:

- ExampleDrug:
  - is metabolized by CYP3A4 via *in-vitro* metabolic rate in the presence of liver microsomes- Michaelis-Menten process with parameters  $K_m = 4 \mu\text{mol/L}$  and  $k_{cat} = 8.761 \text{ 1/min}$ .
  - is metabolized by UGT1A4 via *in-vitro* metabolic rate in the presence of liver microsomes- Michaelis-Menten process with parameters  $K_m = 37.8 \mu\text{mol/L}$  and  $k_{cat} = 4.759 \text{ 1/min}$ .

## Renal/hepatic/biliary kinetics

- ExampleDrug:
  - is cleared renally via glomerular filtration process with parameter GFR fraction = 0.6401.

## Events BB

In the final PBPK model, 3 events were created as listed below:

- Gallbladder emptying enabled.
- High-fat breakfast (from High-fat breakfast template) with Meal energy content 800 kcal (other parameter(s) is(are) as default values in Table 15).
- Urinary bladder emptying with fraction 0.5 enabled.



# Summary

- This work is part of the **Boehringer Ingelheim PBPK Automated Report Generator Project**, which aims to facilitate and accelerate **PK-Sim®-related reporting**.
- The OSP suite R packages serve as a bridge between PK-Sim models and automated reporting workflows.
- **osp.snapshots** R package:
  - Extracts data from PK-Sim BBs and converts them into data frames
  - Enables simulation computation (via `ospsuite` R) and generates simulation plots (teaser in the next slide)

# What's next? Generating simulation plots

## Step 1: running simulations from snapshots + storing the results for faster loading

```
simulations_results <- get_simulations_results(  
  snapshot = snapshot,  
  output_dir =  
  here::here("path/to/simulationResults"),  
  load_results = TRUE  
)
```

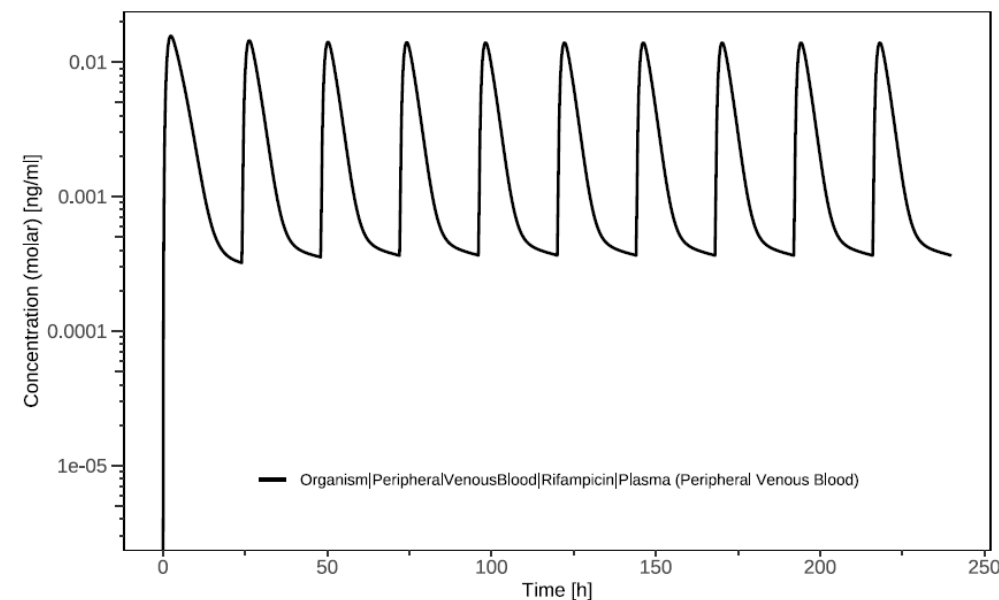
```
"Simulations": [  
  {  
    "Name": "simulation1",  
    "Model": "4Comp",  
    "ObservedData": [...],  
    "Solver": {...},  
    "OutputSchema": [...],  
    "Parameters": [...],  
    "OutputSelections": [...],  
    "OutputMappings": [...],  
    "Individual": "...",  
    "Compounds": [...],  
    "Events": [...],  
    "ObserverSets": [...],  
    ...  
  }  
]
```

There is more to come

ExampleDrug-simulation1.pkml  
ExampleDrug-simulation1-Results.csv  
ExampleDrug-simulation2.pkml  
ExampleDrug-simulation2-Results.csv

## Step 2: plotting time profiles

```
generate_plot( simulations_results = simulations_results,  
               simulation_name = "simulation1",  
               plot_name = "Time Profile Analysis")
```



# Acknowledgement

- Boehringer Ingelheim:
  - Ibrahim Ince
  - PBPK/QSP modeling team members
  - Steve Choy
  - Hugo Maas
  - Jan-Georg Wojtyniak
  
- ESQlabs Software Team & others
  
- OSP community

# Disclaimer

© 2025 Boehringer Ingelheim International GmbH. All rights reserved.

This presentation and its contents are property of Boehringer Ingelheim and are, inter alia, protected by copyright law. Complete or partial passing on to third parties as well as copying, reproduction, publication or any other use by third parties is not permitted.