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Building a Qualifiable MIDD Ecosystem

with modular PBPK and QSP Models in OSP V12

30.09.2025 / OSP CC 2025 /Pavel Balazki

Modularization in OSP

Timeline

- September 2024 – OSMOSES concept presented at OSP CC, beta version available

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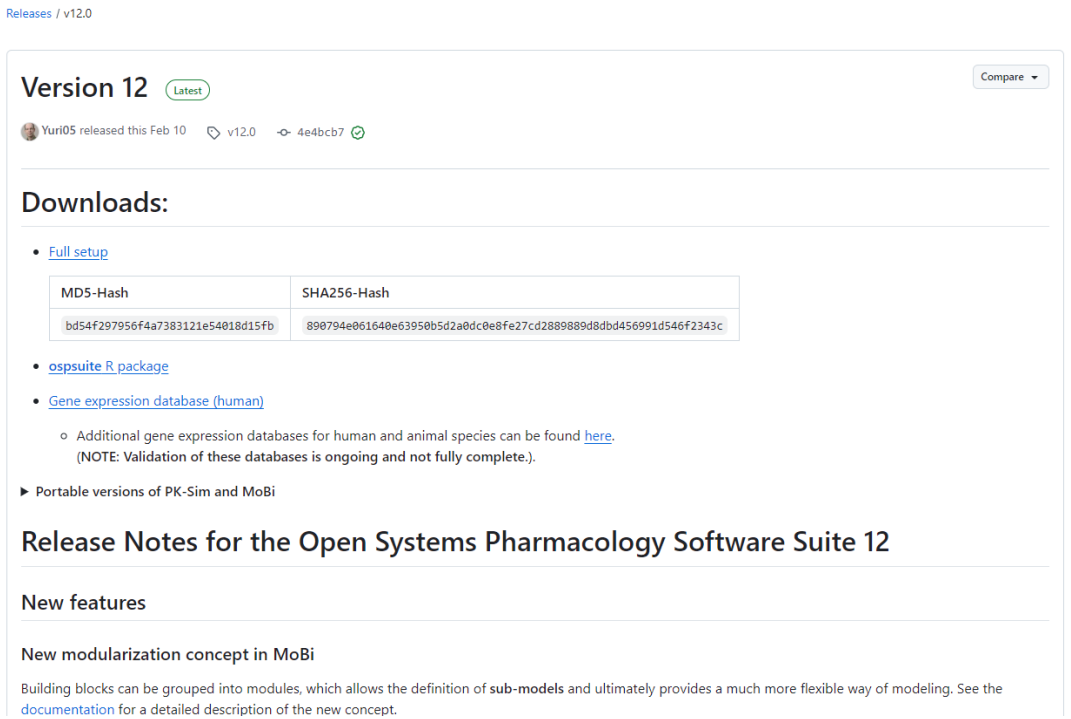
- February 2025 – release of v12



Releases / v12.0

Version 12 Latest

Compare

Yuri05 released this Feb 10 v12.0 4e4bcb7

Downloads:

- Full setup

MD5-Hash	SHA256-Hash
bd54f297956f4a7383121e54018d15fb	890794e061640e63950b5d2a0dc0e8fe27cd2889889d8dbd456991d546f2343c

- ospsuite R package
- Gene expression database (human)
  - Additional gene expression databases for human and animal species can be found here.
    (NOTE: Validation of these databases is ongoing and not fully complete.).

▶ Portable versions of PK-Sim and MoBi

Release Notes for the Open Systems Pharmacology Software Suite 12

New features

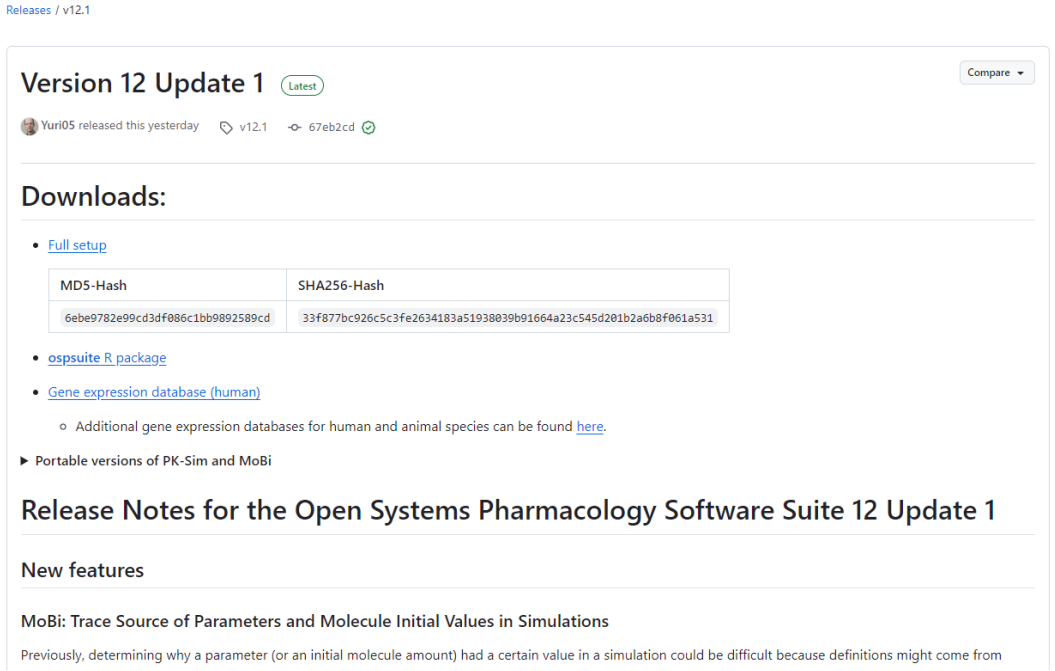
New modularization concept in MoBi

Building blocks can be grouped into modules, which allows the definition of **sub-models** and ultimately provides a much more flexible way of modeling. See the documentation for a detailed description of the new concept.

Modularization in OSP

Timeline

- September 2024 – OSMOSES concept presented at OSP CC, beta version available
- February 2025 – release of v12
- September 2025 – release of 12.1



Releases / v12.1

Version 12 Update 1 Latest

Compare

Yuri05 released this yesterday v12.1 67eb2cd

Downloads:

- Full setup

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▶ Portable versions of PK-Sim and MoBi

Release Notes for the Open Systems Pharmacology Software Suite 12 Update 1

New features

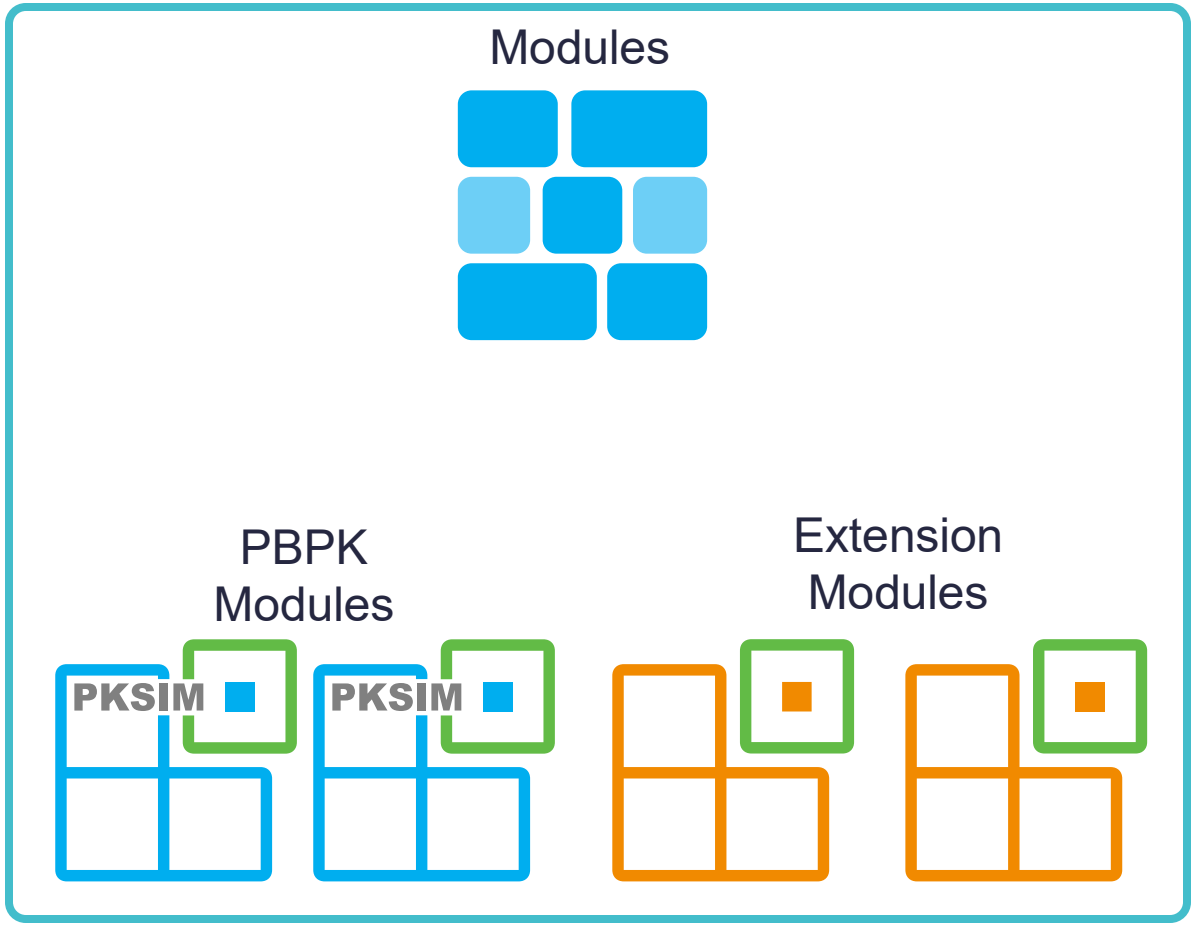
MoBi: Trace Source of Parameters and Molecule Initial Values in Simulations

Previously, determining why a parameter (or an initial molecule amount) had a certain value in a simulation could be difficult because definitions might come from

Modularization in OSP
Quick recap

Project organization

MoBi v12



Individuals

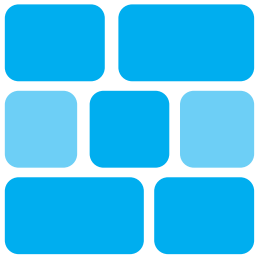
Expression Profiles

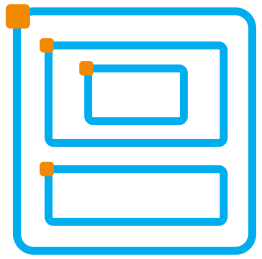
Combined model

Project organization

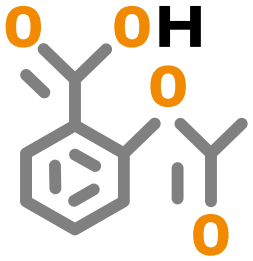
MoBi v12

A module

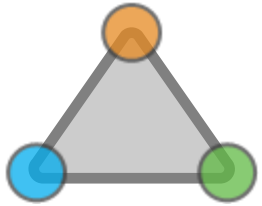




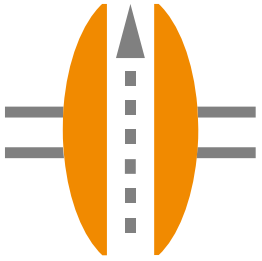
Spatial Structure



Molecules



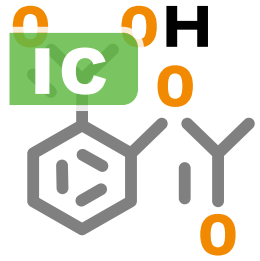
Reactions



Passive Transports

Observers

Events



Initial Conditions

Parameter Values

Project organization

Examples of combination

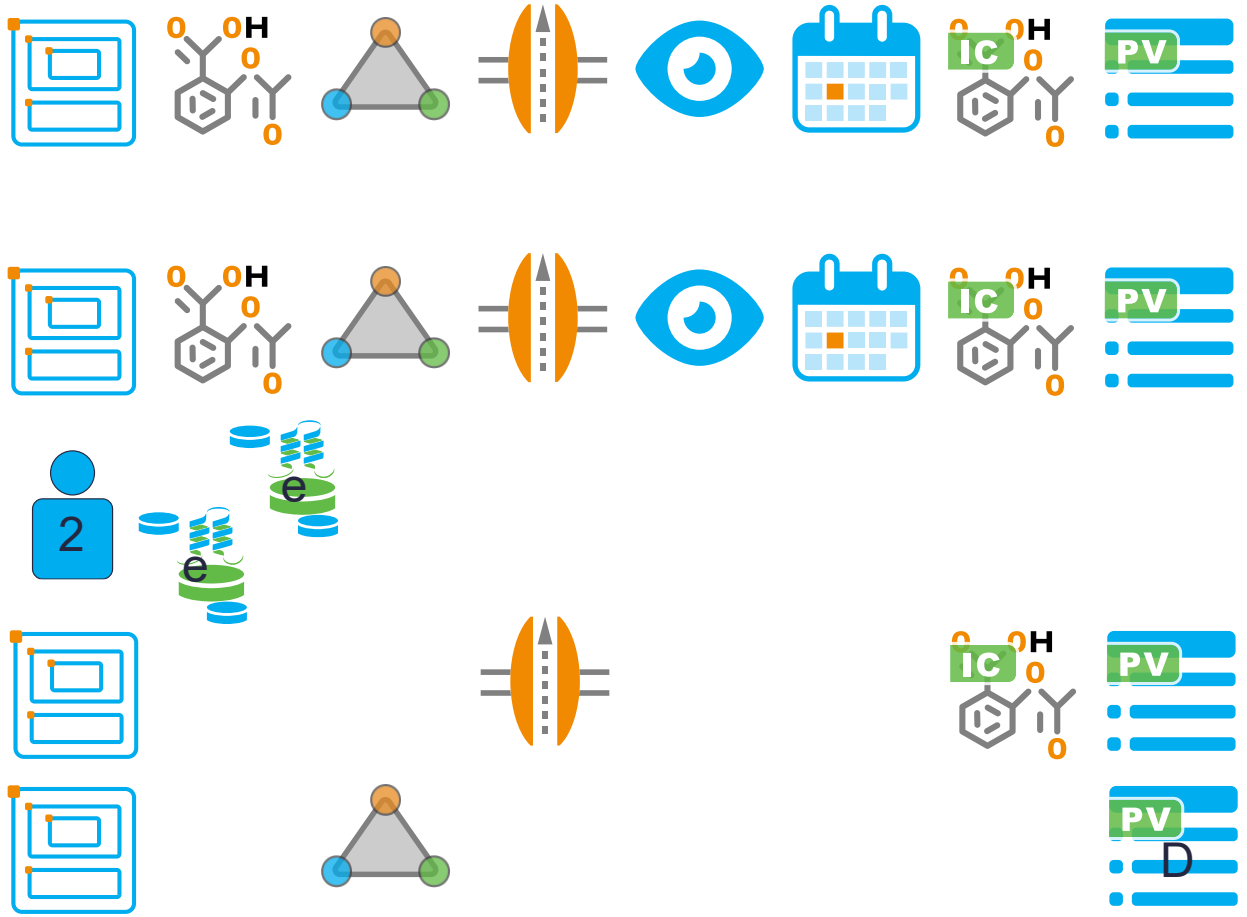
PKSIM CompoundA

PKSIM CompoundB

31 years old female
Extensive metabolizer

Pregnancy

CompoundA effect model
Disease population



After 1 Year of Modularization

Enabling technology, or confusing concept?

Modularization

Defined goals and objectives

Modularization of PB-QSP projects as a solution for

- ? Management of ever-growing model complexity
- ? Model re-usability
- ? Collaborative model development
- ? Community involvement and distribution of models
- ? Automated (re-)qualification of QSP projects

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Modularization

Management of ever-growing model complexity

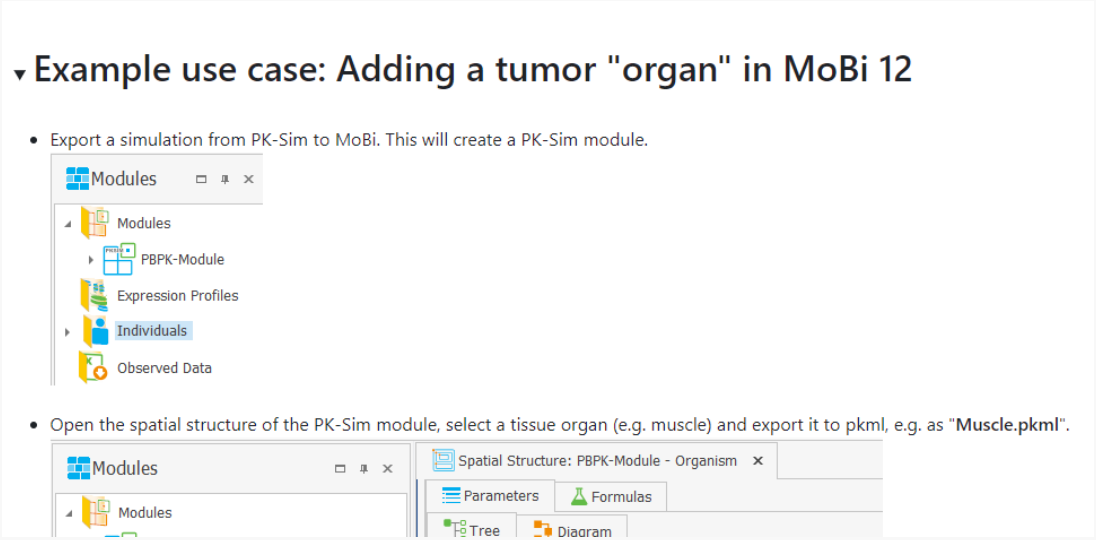
Use case – adding a new organ (e.g., tumor)

V11

- Time effort - 1 hour
- Must be repeated for each project

V12

- Time effort – 15 minutes
- Once created, can be reused!



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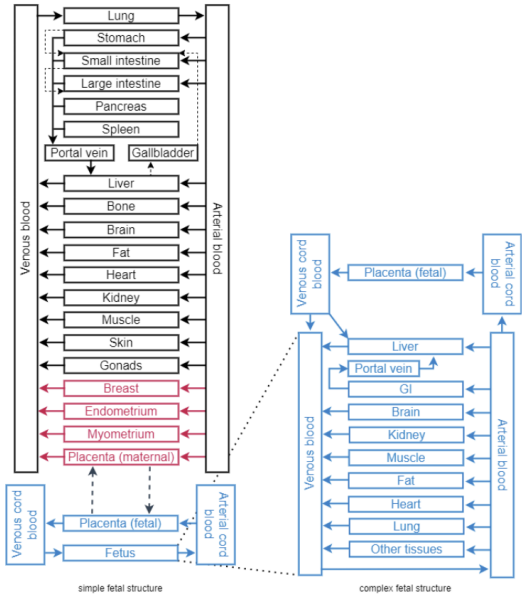
MoBi Modules on GitHub

- Pregnancy modules
  - https://github.com/Open-Systems-Pharmacology/Pregnancy-Models/tree/pregnancy-modules

Within this repository, we distribute MoBi modules of maternal-fetal physiology for whole-body physiologically based (PB) models to simulate the pharmacokinetics (PK) of compounds in pregnant individuals. The modules are based on the PBPK pregnancy models published in [1,2,3,4,5,6,7].

The pregnancy model structure comprises 27 compartments by default, including nine pregnancy-specific compartments, as shown in the schema below.



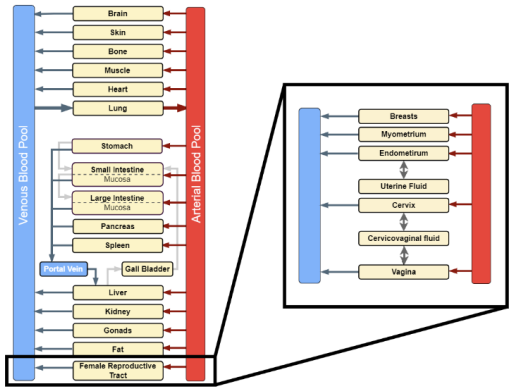
MoBi Modules on GitHub

- Pregnancy modules
  - https://github.com/Open-Systems-Pharmacology/Pregnancy-Models/tree/pregnancy-modules
- Female reproductive tract
  - https://github.com/Open-Systems-Pharmacology/Female-Reproductive-Tract-PBPK-Module
- Lactation module
  - In development

Female Reproductive Tract

Within this repository, we distribute MoBi® modules for the female reproductive tract. The module is an extension of the whole-body physiologically based pharmacokinetic models developed in Open Systems Pharmacology. The extension module can be used to simulate transfer of medicines towards female reproductive tract organs, or to simulate pharmacokinetics of compounds after local administration..

The extension module consists of five tissue compartments (endometrium, myometrium, vagina, cervix and breasts) and two fluid compartments (uterine fluid and cervicovaginal fluid) that can be added to a PBPK base model. This module does not consider the external part of the female reproductive tract. Furthermore, ovaries and fallopian tubes are not included due to lack of data. All tissue compartments have the same sub-compartmentalization as the tissues of the base whole-body structure.



More modules in development

Not publicly available (yet)

- Dissolution models (e.g., Z-Factor dissolution model, to be added to PK-Sim)
- Administration routes (sc, inhalation, …)
- Target-Mediated Drug Disposition (TMDD)
- Organ modules (Tumor, lymph nodes, CNS)
- Mechanistic plasma protein binding
- … and many more!

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- ✓ Community involvement and distribution of models
- ? **Automated (re-)qualification of QSP projects**
- ? **Building a MIDD Ecosystem**

Model Informed Drug Development Ecosystem

MIDD Ecosystem

Paradigm shift

From managing isolated models

to

Maintaining a (growing) Ecosystem of Models, Modules, and Workflows

MIDD Platform Management

An end-to-end qualified modular modeling Ecosystem

(Community-built)
models & modules

PBPK models library

PK-Sim®

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PBPK Model

PBPK LifeCycle

PBPK projects

ADMET-HT-PBPK, IVIVE, FiH, DDI, PBBM/CMC, Spec. Pops...

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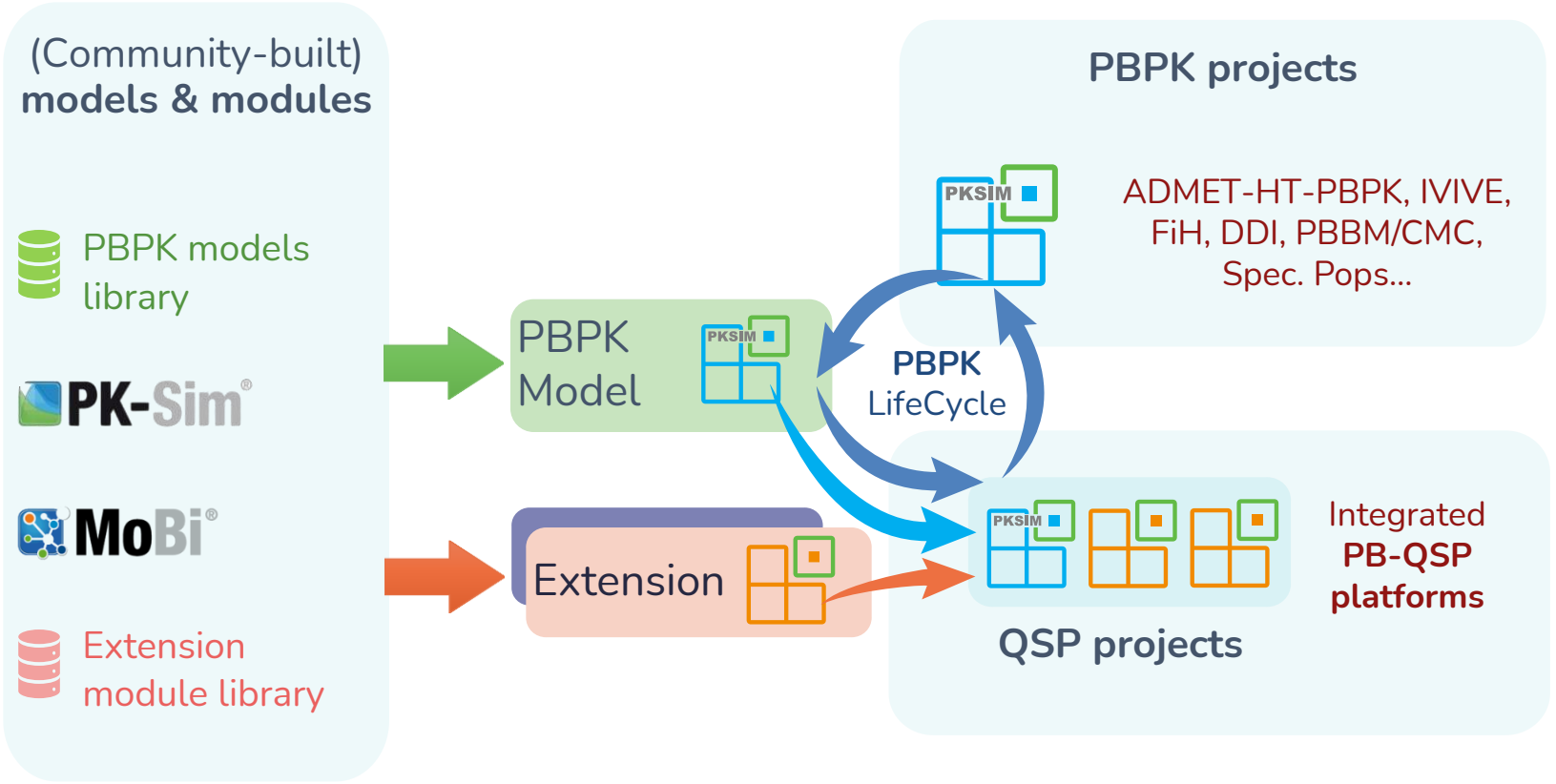

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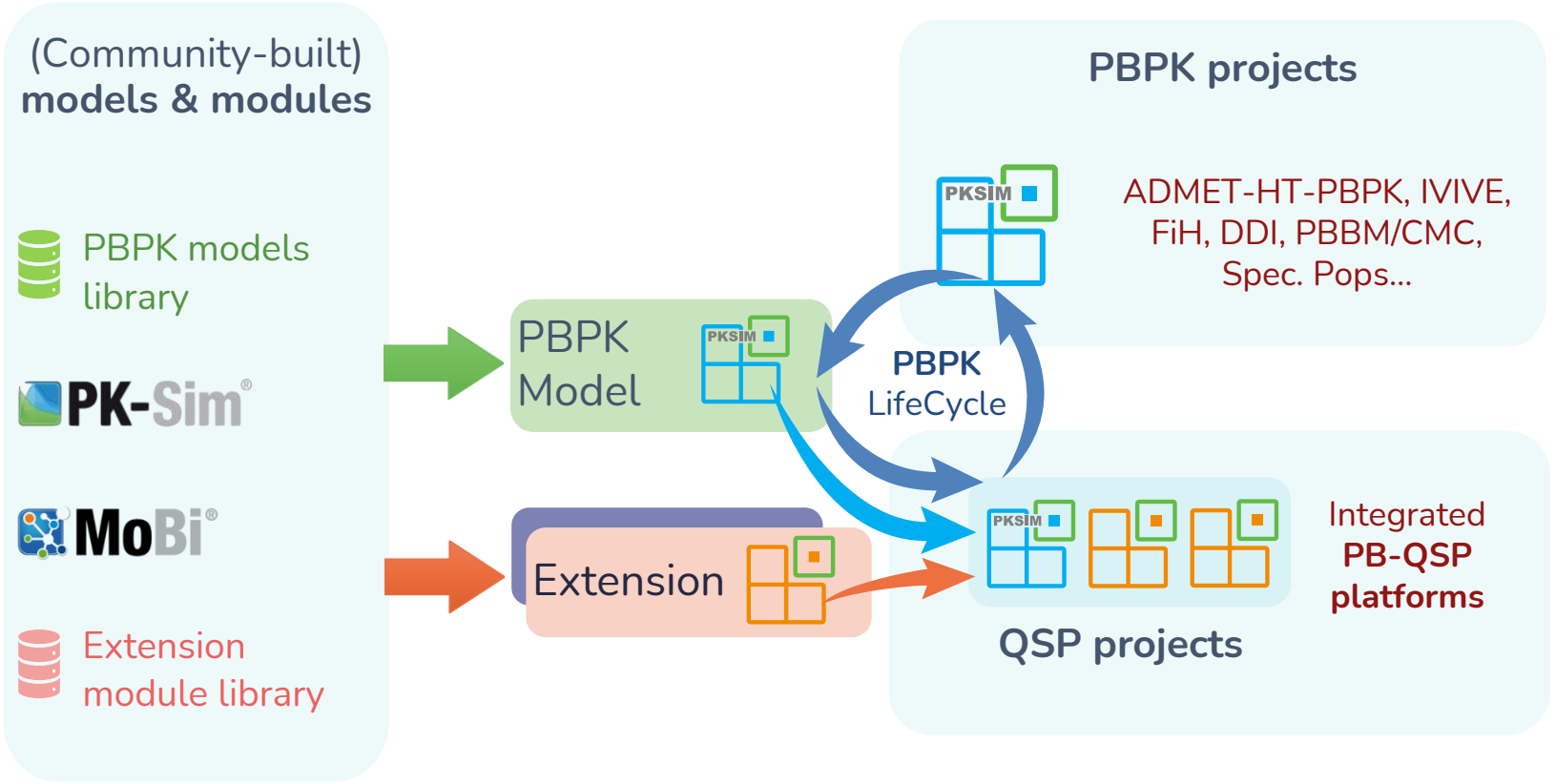

PBPK Model LifeCycle easily integrated into QSP Projects thanks to “PK-Sim” modules”

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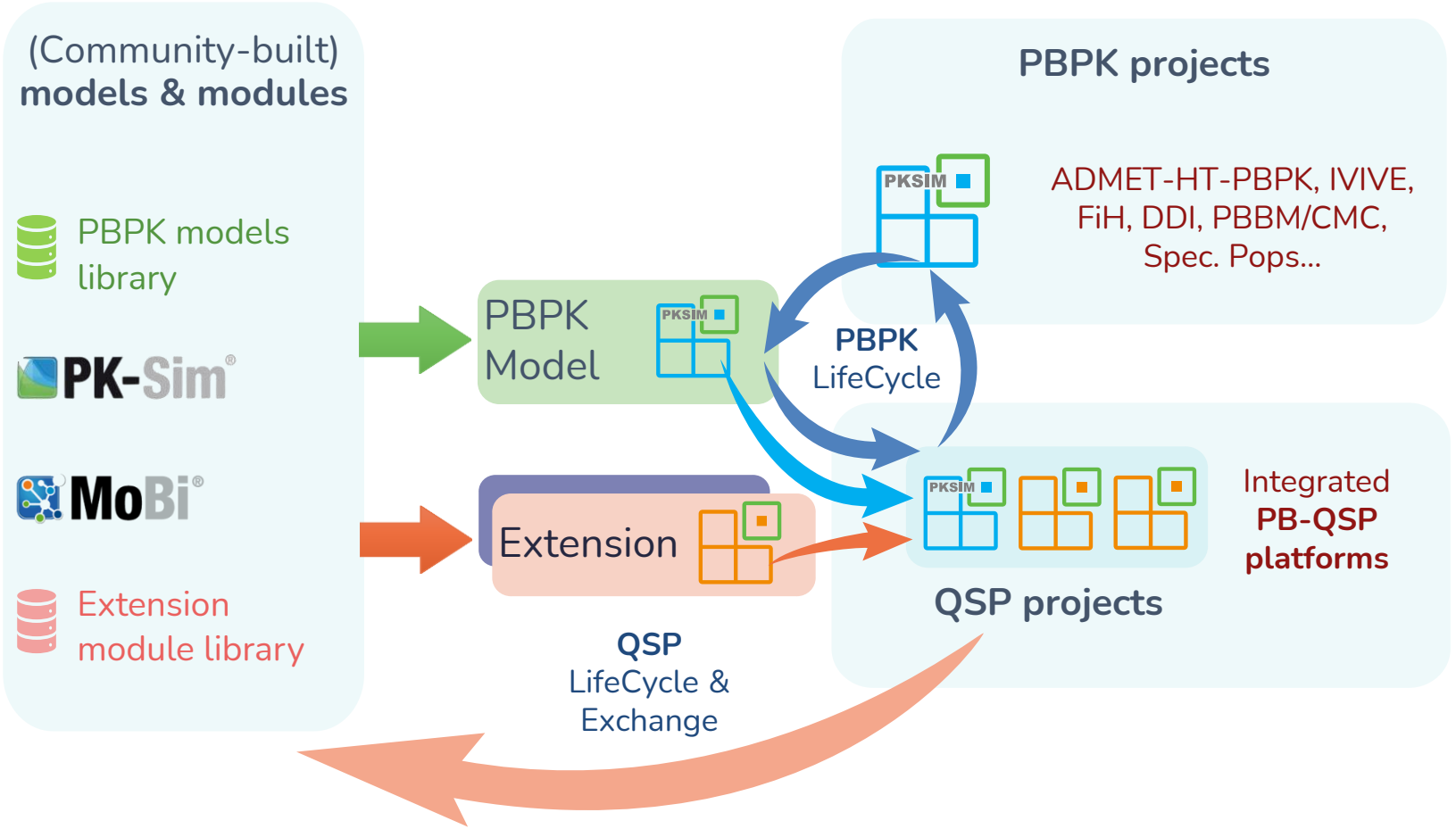

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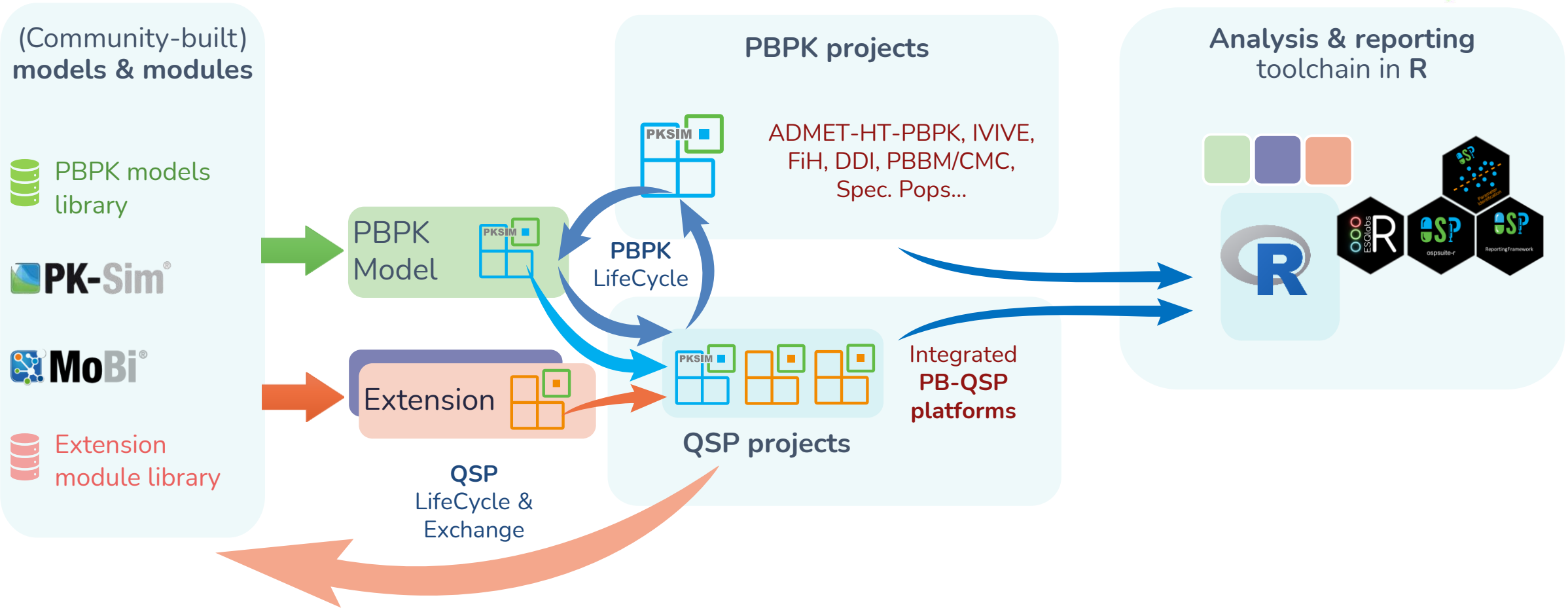

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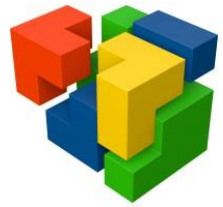


(Community-built) **models & modules**

PBPK models library

PK-Sim®

MoBi®

Extension module library

PBPK Model

Extension

QSP LifeCycle & Exchange

PBPK LifeCycle

PBPK projects

ADMET-HT-PBPK, IVIVE, FiH, DDI, PBBM/CMC, Spec. Pops...

QSP projects

Integrated **PB-QSP platforms**

Analysis & reporting toolchain in **R**

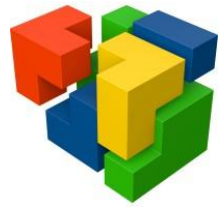
Qualification Framework

Qualification Report

Modularization workflows

MIDD Platform Management

An end-to-end qualified modular modeling Ecosystem



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QSP projects

Integrated **PB-QSP platforms**

Analysis & reporting toolchain in **R**

Qualification Report

Qualification Framework

MoBi.R

{ospsuite} R package will support MoBi projects in v13

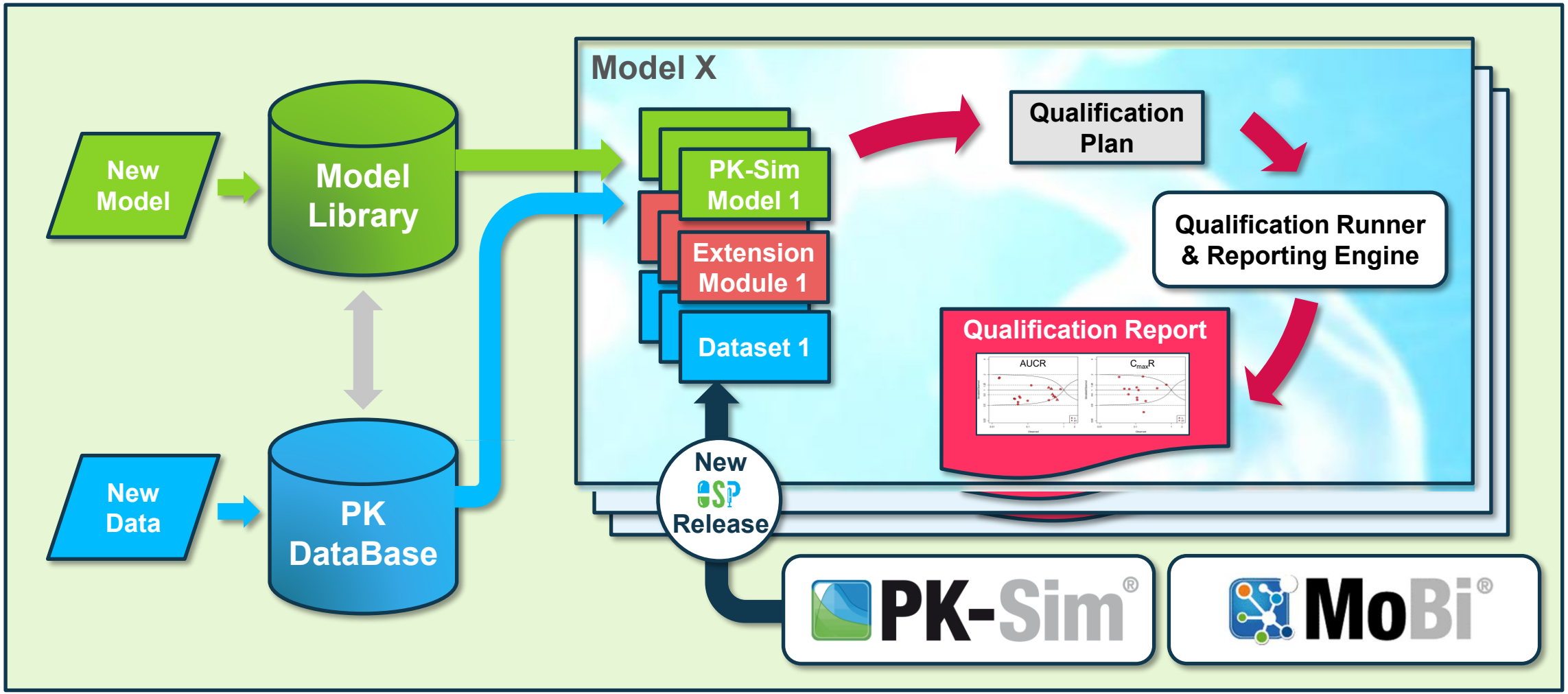
R workflows will support:

- Loading of MoBi Projects
- Creating simulations from available modules
- Creating new individuals, expression profiles
- Loading modules from PKML
- Adjusting parameter values, adding new parameters, setting initial conditions

Re-qualification of QSP Models

Platform Qualification: Automatic (Re)-qualification Workflow

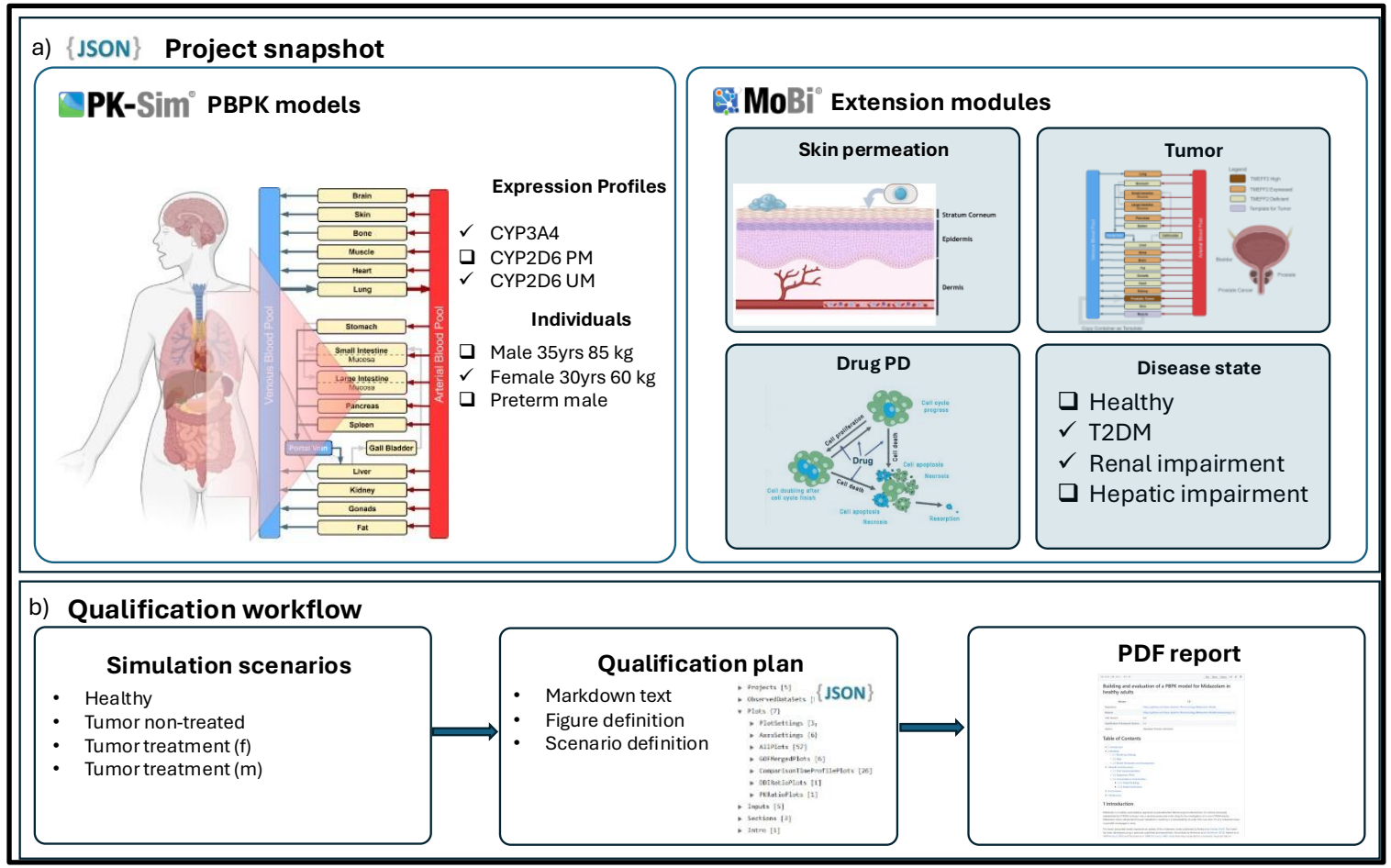
Sustainable and Agile (Re)-Qualification of Intended Use Scenarios for Regulatory Submissions



QSP Platform Qualification

MoBi Project Snapshot

- Key aspect is the **MoBi project snapshot**
  - PK-Sim modules snapshot(s)
  - Extension modules as pkml
  - Observed data
  - Model configurations & models
    - List of all user-defined (parameter) values
- RQ Workflow:
  - Re-create PK-Sim modules
  - Re-create Individuals and Expression Profiles
  - Re-create model configurations & models
  - Apply user-defined values
  - Simulate and compare to observed data
  - Create Qualification Report



Summary

Modularization for Modeling Ecosystem

- Growing number of (PBPK) **Models** and (QSP) **Modules** available in the community

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- Automated **re-qualification** of MoBi projects in OSP v13

- Growing number of (PBPK) **Models** and (QSP) **Modules** available in the community
- **MoBi.R** – R interface to turn **modules** to ready-to-use **solutions**
- Automated **re-qualification** of MoBi projects in OSP v13
- … will enable to build an ecosystem of re-usable, qualified models

Thank you!

Pavel Balazki, Stephan Schaller

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