Software Verification, Validation, and (CoU) Qualification of Open Source M&S Software

for Regulatory Use in Translational Model-Informed Drug Development

Stephan Schaller, on behalf of the OSP Management Team
(Jörg Lippert, Rolf Burghaus, Ibrahim Ince, Andreas Kovar, Lars Küpfer, Thorsten Lehr, Stephan Schaller, Jan Schlender, Michaël Sevestre, Erik Sjögren, Juri Solodenko, Alexander Staab, and Donato Teutonico)

Conflict of Interest Disclosure

The presenter, Stephan Schaller, holds the following positions:

- Chair, Open Systems Pharmacology (OSP) Management Team (www.open-systems-pharmacology.org)
- Founder and Chief Executive Officer, ESQlabs GmbH
    - ESQlabs GmbH is a contract research organization that incorporates the OSP Suite as part of its commercial service portfolio.

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The Challenge: Regulatory Qualification in MIDD

Why mechanistic models need robust verification & validation

Requirements of Mechanistic Model-based Assessment in a Regulatory Context

TRACEABLE

Models allow traceability of data, assumptions, and parameters across molecules (and species).

ACCESSIBLE

Open-access, shared libraries, ensuring equitable access and trust

MECHANISTIC

Enabling confidence in knowledge-based extrapolation across data gaps

REPRODUCIBLE

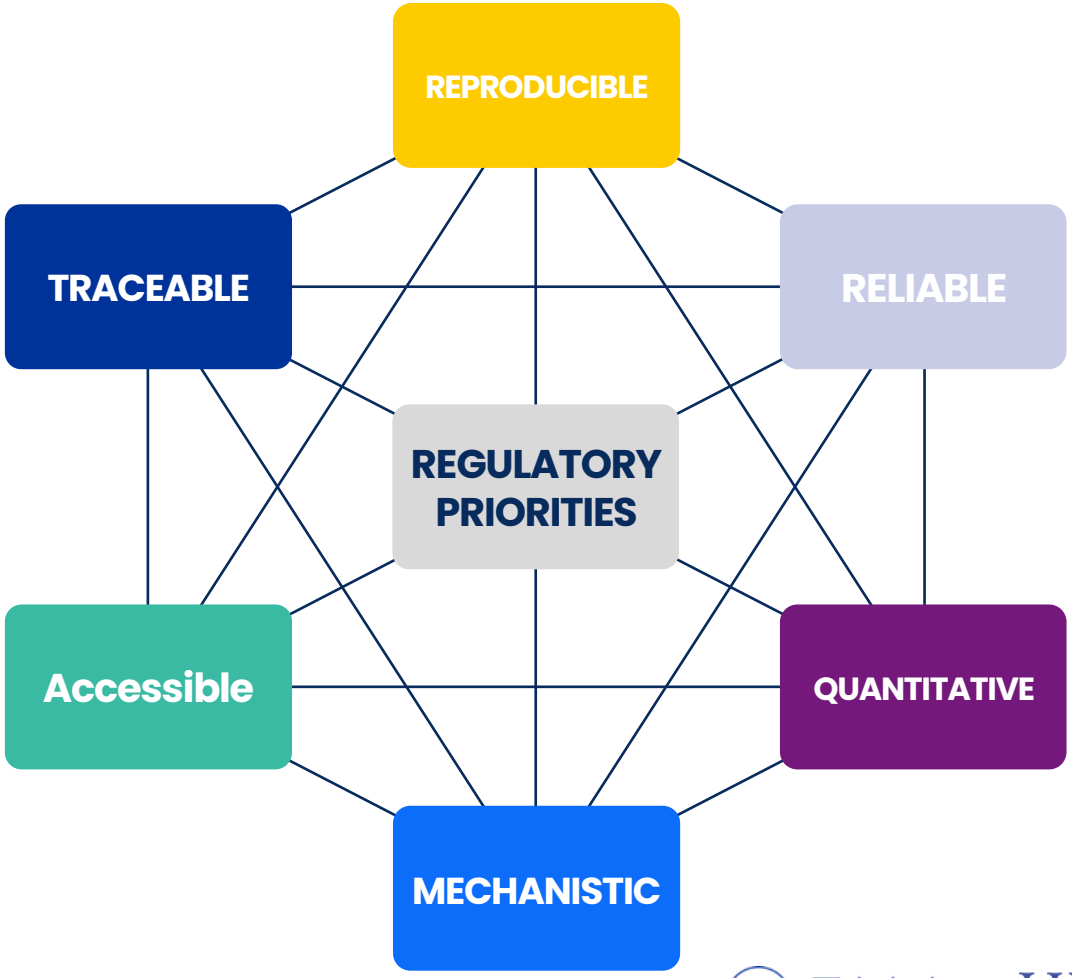
Transparent, reproducible predictions strengthen regulatory confidence.

RELIABLE

Continuous validation, automated testing and multi-institutional verification

QUANTITATIVE

Support quantitative, human-relevant decision making.



The Regulatory Challenge

Mechanistic models are pivotal but face qualification hurdles

The Qualification Paradox

The Promise

- Mechanistic models are pivotal for MIDD
- FDA & EMA guidances endorse PBPK/QSP use
- Regulatory decisions increasingly model-informed

✓ Growing acceptance

! Great responsibility

The Reality

- No universal qualification framework established
- Platform performance verification unclear
- Version control & lifecycle management complex
- Transparency requirements challenging??

⚠ Implementation barriers

“These challenges exceed any individual organization's capacity"

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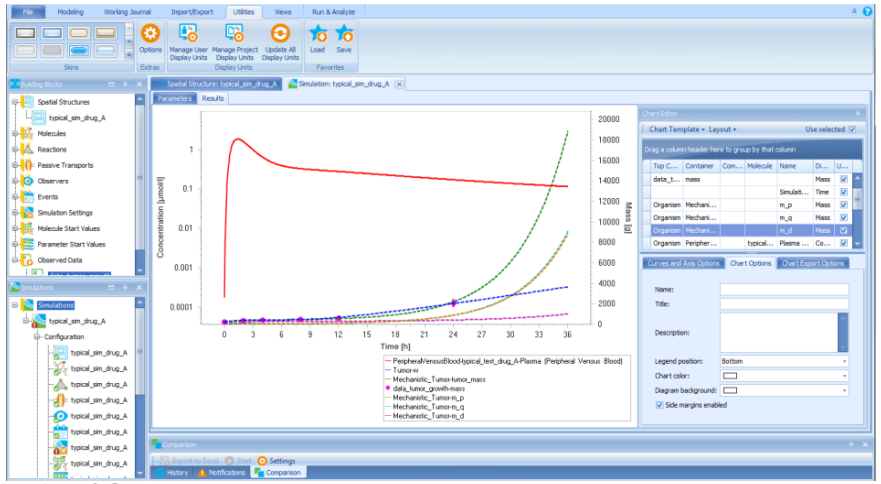
Transparent Infrastructure: GitHub Ecosystem

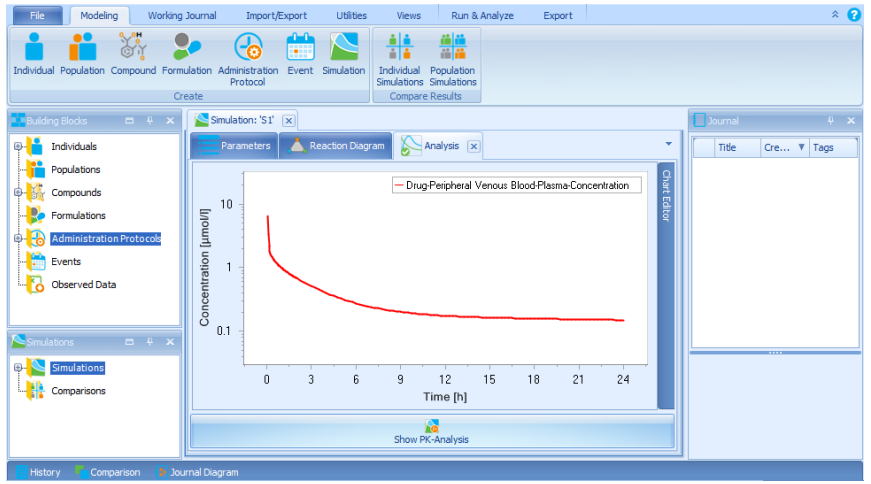
How open source enables continuous validation & community review

Open Systems Pharmacology Suite: PK-Sim® & MoBi®:

An **open-source** multiscale Physiologically-Based & **Mechanistic Modeling** platform which has been developed and refined for **20 years**!

MoBi® & PK-Sim® = OSP OPEN SYSTEMS PHARMACOLOGY





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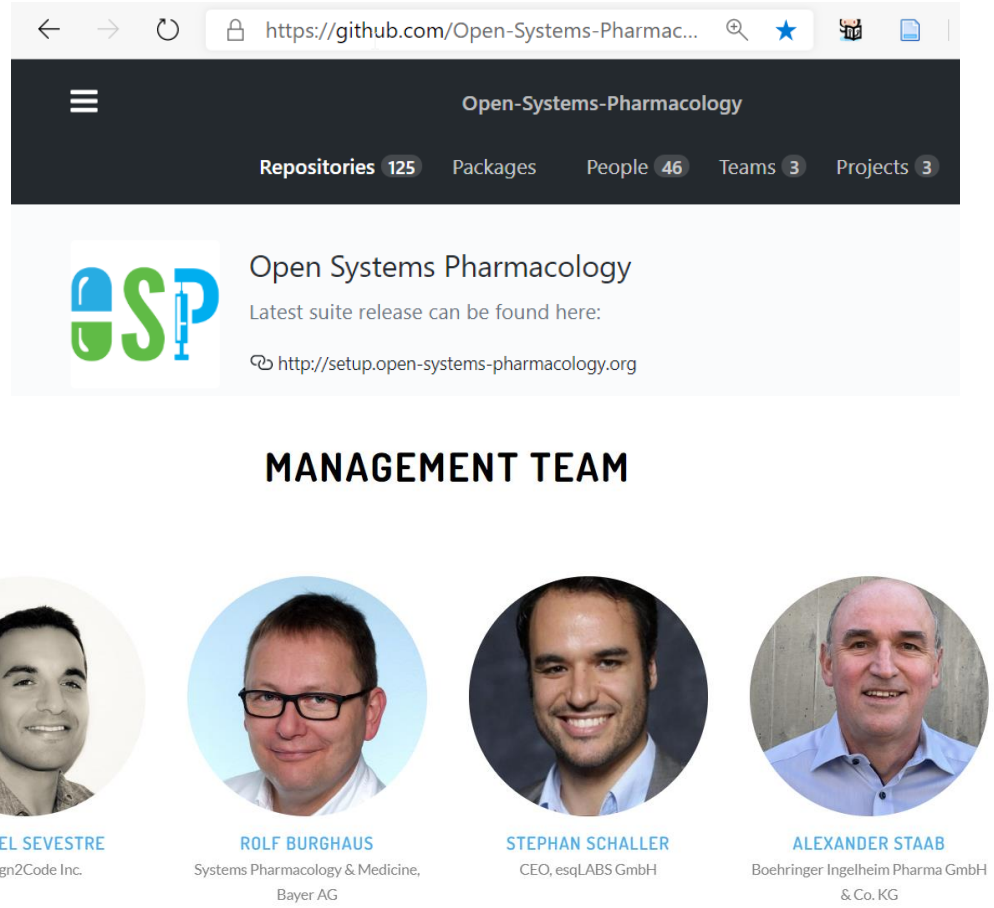
The OSP's Philosophy on Openness
Open Access, Open Source, and Open Science



Open Source since 2017 on GitHub

8+ releases, GPLv2 license

esqlabs
we empower life sciences
SANOFI
Boehringer Ingelheim
BAYER
NOVARTIS
DESIGN{2}CODE
RWTH AACHEN UNIVERSITY
UNIVERSITÄT DES SAARLANDES
Pharmetheus
Pharmacometrics Consulting Services

http://www.open-systems-pharmacology.org/

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The OSP's Philosophy on Openness
Mission & Vision

OSP Roadmap

The OSP Roadmap builds on the Vision & Mission of Open Systems Pharmacology

Vision

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.

Mission

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's Philosophy on Openness

Community-driven development model (Donations across components)

- 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
- CNS

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

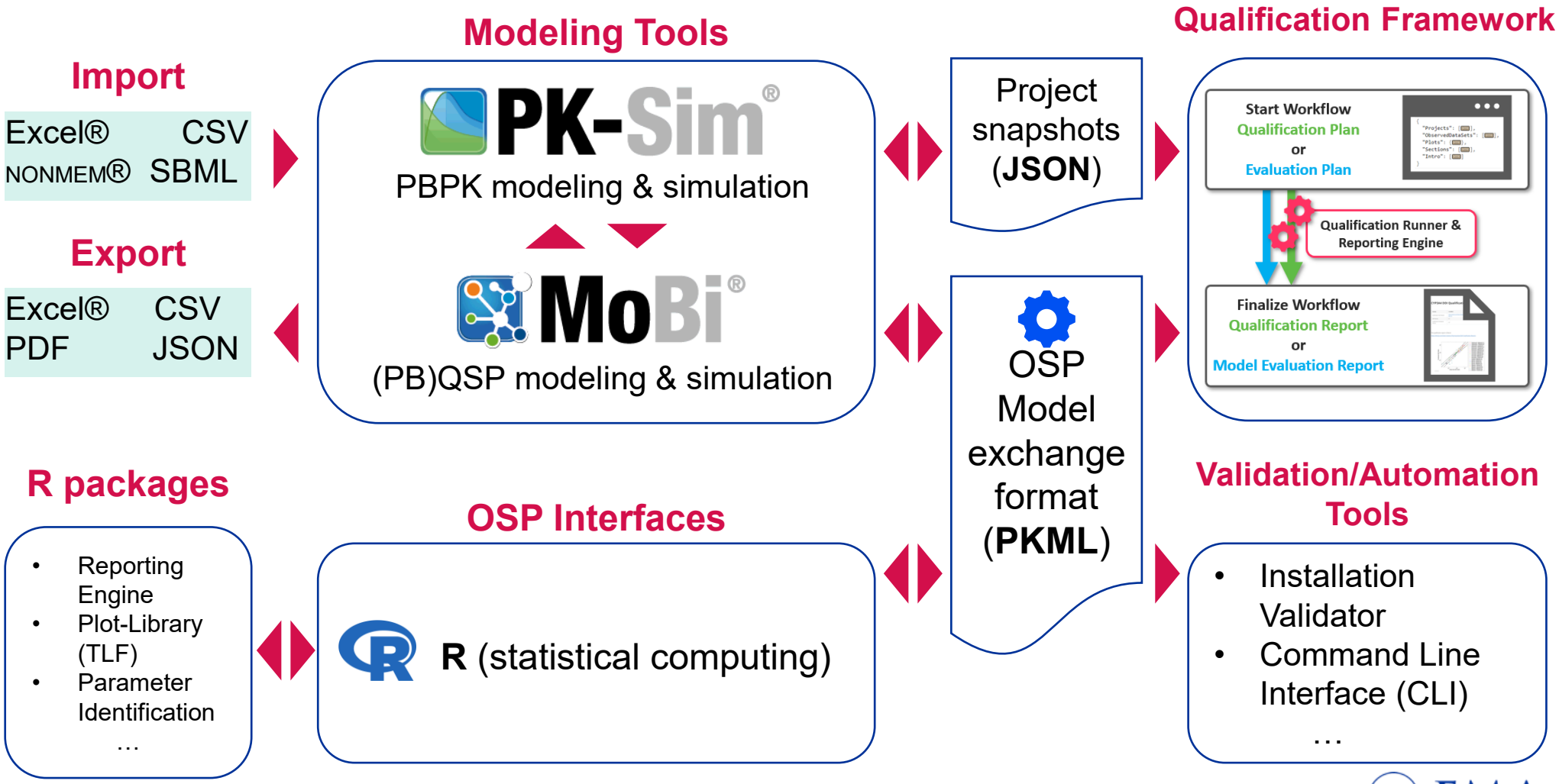
Focus groups shall be the owner of the development in the respective focus area, they are expected to conceptualize and coordinate activities of the respective field.

DDI	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 assess population variability and uncertainty in prior knowledge and posterior results.	Christian Diedrich (@DiedrichC)

OSP's Three Pillars of Trust

- Software Validation
- CoU Qualification
- Installation Verification

The OSP Suite Architecture: PK-Sim, MoBi & R components



PBPK: Physiologically based pharmacokinetic
(PB)QSP: (Physiologically based) Quantitative systems pharmacology

TLF: Tables, listings and figures

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Quality Assurance of the OSP Suite
Continuous Software Validation & Qualification

*OSP Suite is an open-source platform that is developed in a fully transparent manner on **GitHub** (the largest hosting platform for open-source software).*

Two main steps are used to ensure the quality of the OSP Suite: **Validation** and **Qualification.**

- **Platform Validation**: the process of confirming that the software does what it is intended to do:

  → verifying that the software correctly performs calculations and simulations based on the underlying physiological and pharmacokinetic principles.

- **Platform Qualification** for intended use:

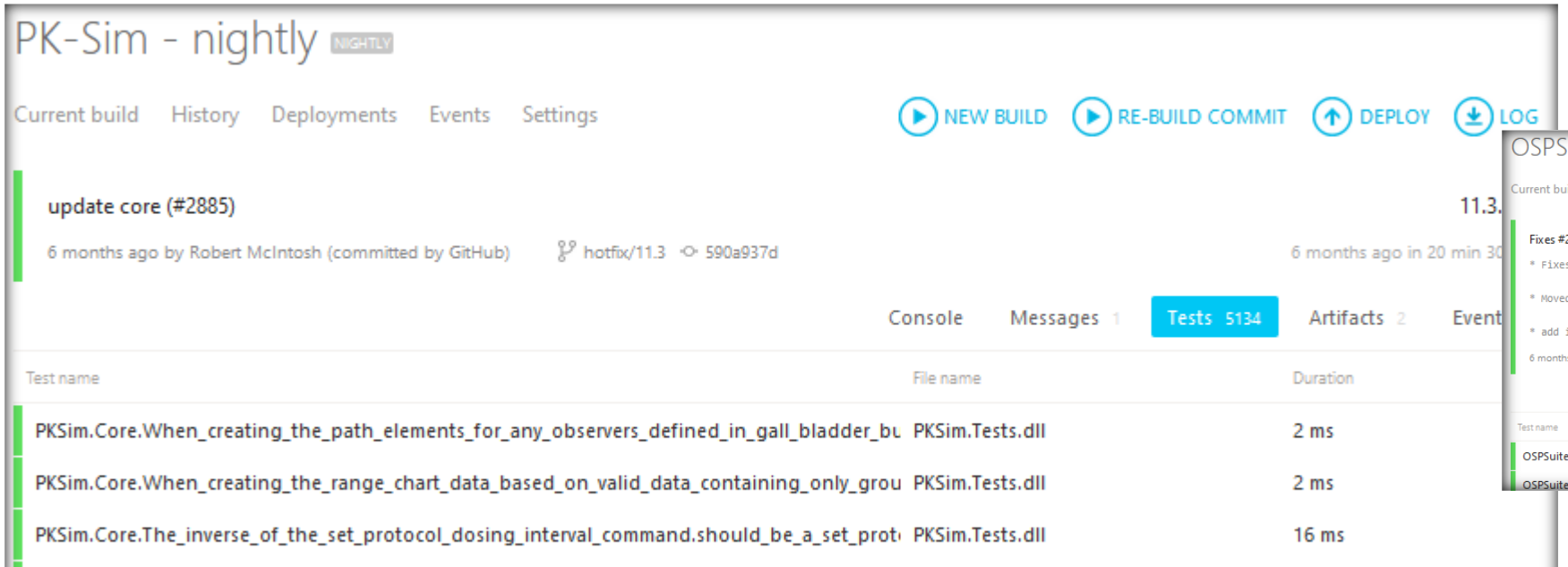
  → assessment of the platform's features, functionalities, and performance metrics in the context of specific use cases.

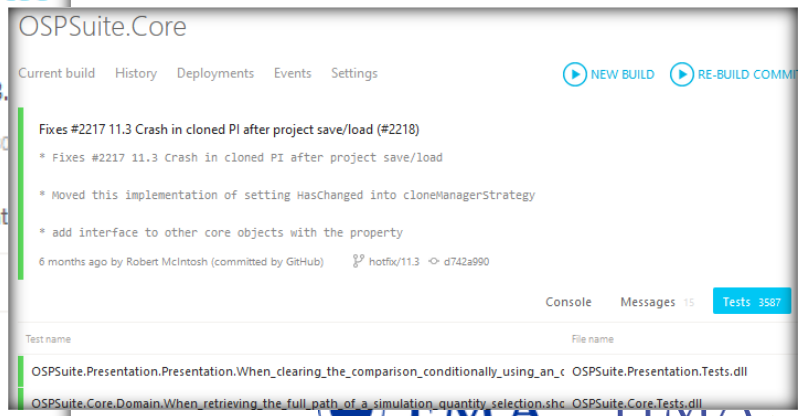
  → e.g., if a platform is intended to predict DDIs, qualification would include demonstrating that it can accurately model and predict these interactions for a range of compounds.

Continuous Software Validation

A growing, extensive library of test cases tested with validated programs

1. Automated testing of the correct behavior of software modules.
   - Tests (unit tests, integration tests...) are triggered with every software build (e.g. about 11600 automated tests for the 11.3 release).
   - New changes are integrated only if all tests are passed.
   - Full test logs for every software build and release are documented on GitHub and available for anyone to view.





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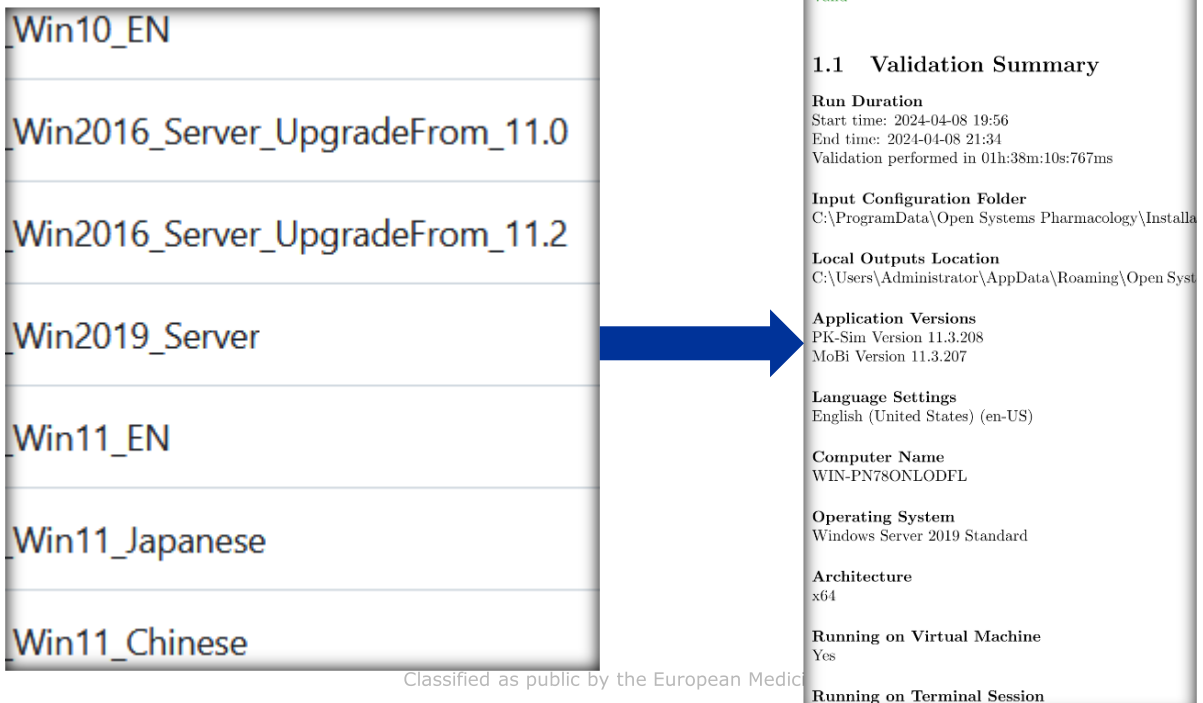
2. Automated comparison of simulation results between software versions for specific combinations of compounds, organisms, calculation methods and model options..

	File	Modell	Simulations		Individual							Compound					Application		
1																			
2			155	Params	Population	Gender	Age	Aging	Enzymes	Transp.	Bind.	Type	pKa	Partition	Permeab.	Process	Dosing	Type	Formulation
43	Human_SingleORAL_Weibull_AsSuspention	4Comp	3	fu/MW/Lipo	ICRP_2002	MALE	30	---	---	---	---	small	Acid	RR	Standard		Single	Oral	Weibull
44	Human_UncompetitiveInhibition	4Comp		---	ICRP_2002	MALE	30		CYP3A4			small	Acid	RR	Standard	Specific_MM CYP3A4	DI_12_12	IntravenousBolus	
45			1	---				---		---	---	small	Acid	RR	Standard	UncompetitiveInhibition CYP3A4	DI_6_6_6_6	IntravenousBolus	
46	Minipig_SingleORAL_Dissolved	4Comp	3	fu/MW/Lipo	Minipig	---	---	---	---	---	---	small	Acid	RR	Standard		Single	Oral	Dissolved
47	Monkey_SingleORAL_Dissolved	4Comp	3	fu/MW/Lipo	Monkey	---	---	---	---	---	---	small	Acid	RR	Standard		Single	Oral	Dissolved
48	Mouse_SingleORAL_Dissolved	4Comp	3	fu/MW/Lipo	Mouse	---	---	---	---	---	---	small	Acid	RR	Standard		Single	Oral	Dissolved
49	Preterm_SingleIV_Age_0_GA_32_CYP3A4	4Comp	1	---	Preterm	MALE	0	X	CYP3A4	---	---	small	Acid	RR	Standard	1stOrder CYP3A4	Single	IntravenousBolus	
50	Preterm_SingleIV_Age_0_GA_32_GFR	4Comp	1	---	Preterm	MALE	0	X	---	---	---	small	Acid	RR	Standard	GFR	Single	Intravenou	Dissolved
51	Preterm_SingleIV_Age_15_GA_32_CYP3A4	4Comp	1	---	Preterm	MALE	0,25	X	CYP3A4	---	---	small	Acid	RR	Standard	1stOrder CYP3A4	Single	IntravenousBolus	
52	Preterm_SingleIV_Age_15_GA_32_GFR	4Comp	1	---	Preterm	MALE	0,25	X	---	---	---	small	Acid	RR	Standard	GFR	Single	Intravenou	Dissolved
53	Rabbit_SingleORAL_Dissolved	4Comp	3	fu/MW/Lipo	Rabbit	---	---	---	---	---	---	small	Acid	RR	Standard		Single	Oral	Dissolved
54	Rat_MultiORAL_6_6_6_6_Dissolved	4Comp	1	---	Rat	---	---	---	---	---	---	small	Acid	RR	Standard		DI_6_6_6_6	Oral	Dissolved
55	Rat_MultiORAL_6_6_12_Dissolved	4Comp	1	---	Rat	---	---	---	---	---	---	small	Acid	RR	Standard		DI_6_6_12	Oral	Dissolved
56	Rat_MultiORAL_8_8_8_Dissolved	4Comp	1	---	Rat	---	---	---	---	---	---	small	Acid	RR	Standard		DI_8_8_8	Oral	Dissolved
57	SingleIV_2Pores_Human	TwoPores	4	Kd (FcRn)_endo C_FcRn_endo(0)	ICRP_2002	MALE	30	---	---	---	---	Large	Acid	Standard	Standard		Single	IntravenousBolus	
58	SingleIV_2Pores_Monkey	TwoPores	3	Kd (FcRn)_endo C_FcRn_endo(0)	Monkey	---	---	---	---	---	---	Large	Acid	Standard	Standard		Single	IntravenousBolus	
59	SingleIV_2Pores_Mouse	TwoPores	4	Kd (FcRn)_endo C_FcRn_endo(0)	Mouse	---	---	---	---	---	---	Large	Acid	Standard	Standard		Single	IntravenousBolus	
	SingleIV_C1_4Comp																		

Continuous Software Validation

A growing, extensive library of test cases tested with validated programs

1. Automated testing of the correct behavior of software modules.
2. Automated comparison of simulation results between software versions for specific combinations of compounds, organisms, calculation methods and model options.
3. Automated testing in different software environments (different operating systems, etc.).



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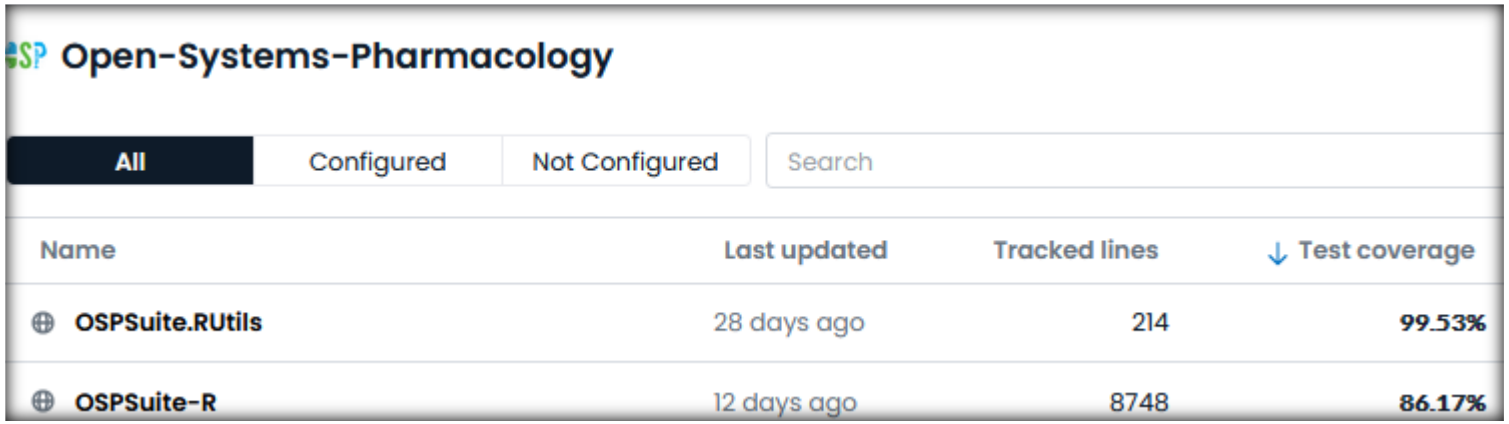
4. Automated code quality analysis (e.g. static code analysis, test coverage).



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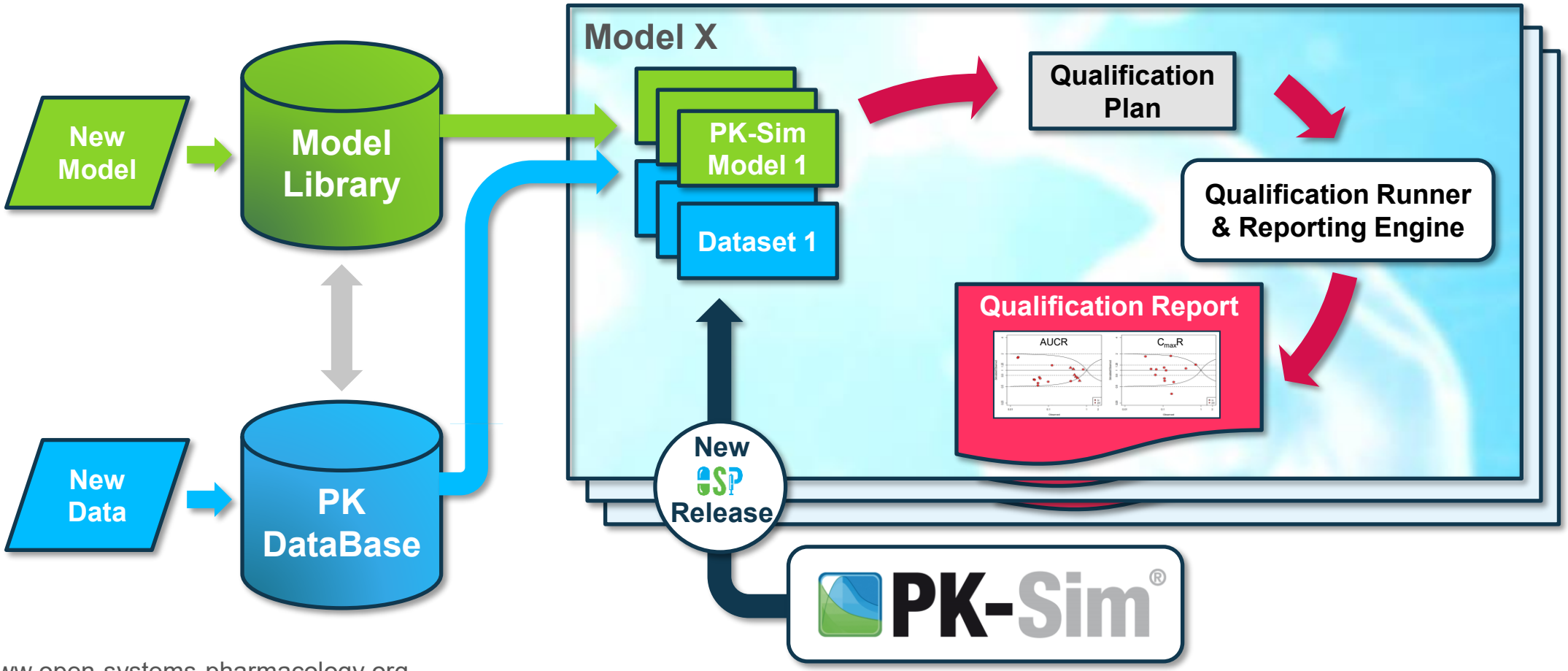
3. Automated testing in different software environments (different operating systems, etc.).
4. Automated code quality analysis (e.g. static code analysis, test coverage).
5. (Manual) testing of new features by scientific experts.

Community-Driven CoU Qualification Framework

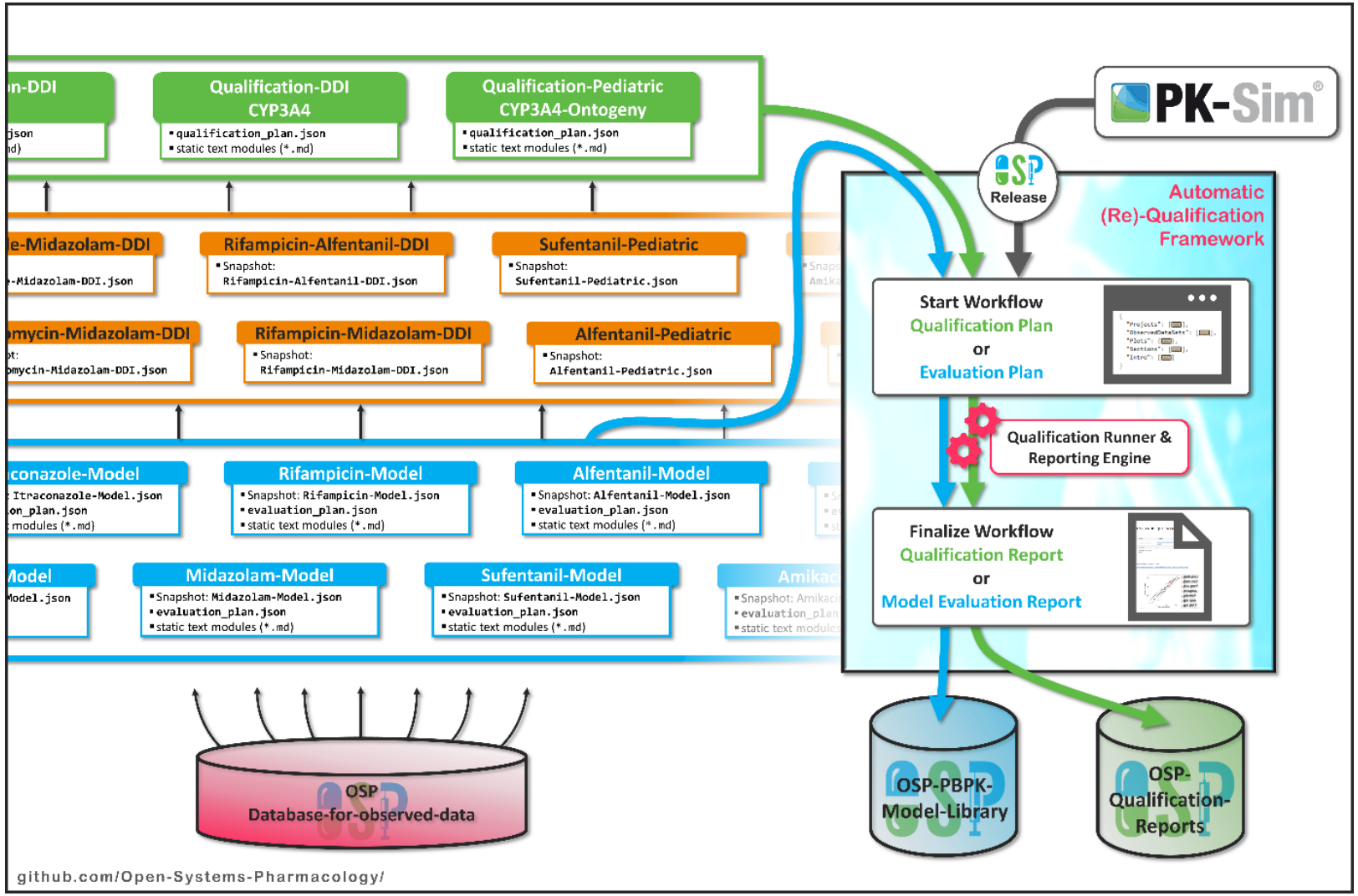
Automatic (Re)-qualification Workflow



www.open-systems-pharmacology.org

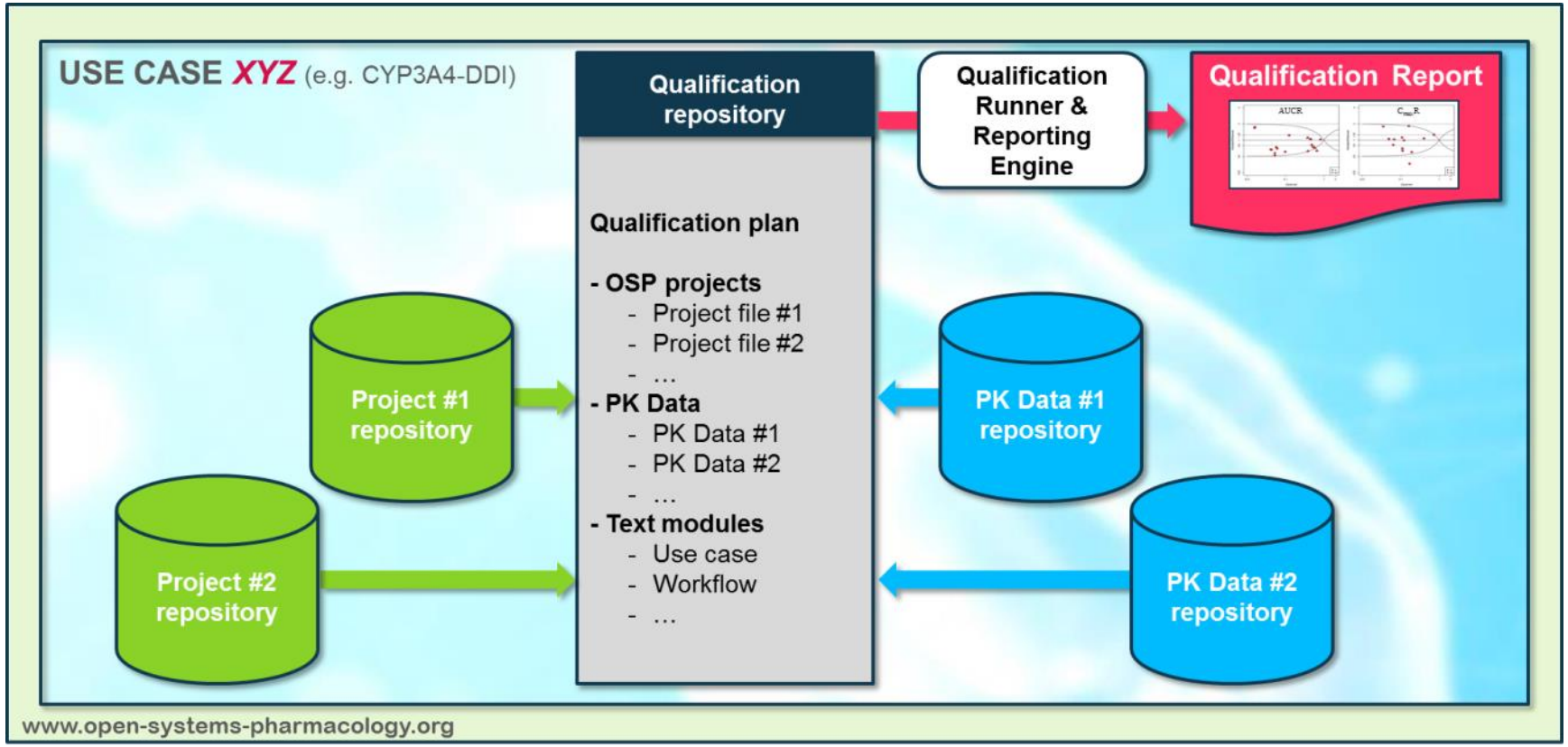
Community-Driven CoU Qualification Framework
Qualification Repository Structure

- Repository landscape with the embedded qualification framework.
- Various input repositories:
  - Blue: model repositories for single PBPK substance models (including a snapshot file and an evaluation plan),
  - Orange: dependent (intermediate) model repositories needed for specific qualification scenarios (including a snapshot file for specific simulation set-up),
  - Green: qualification repositories for specific qualification purposes, pink container
- The framework extracts PK data from the hosted database



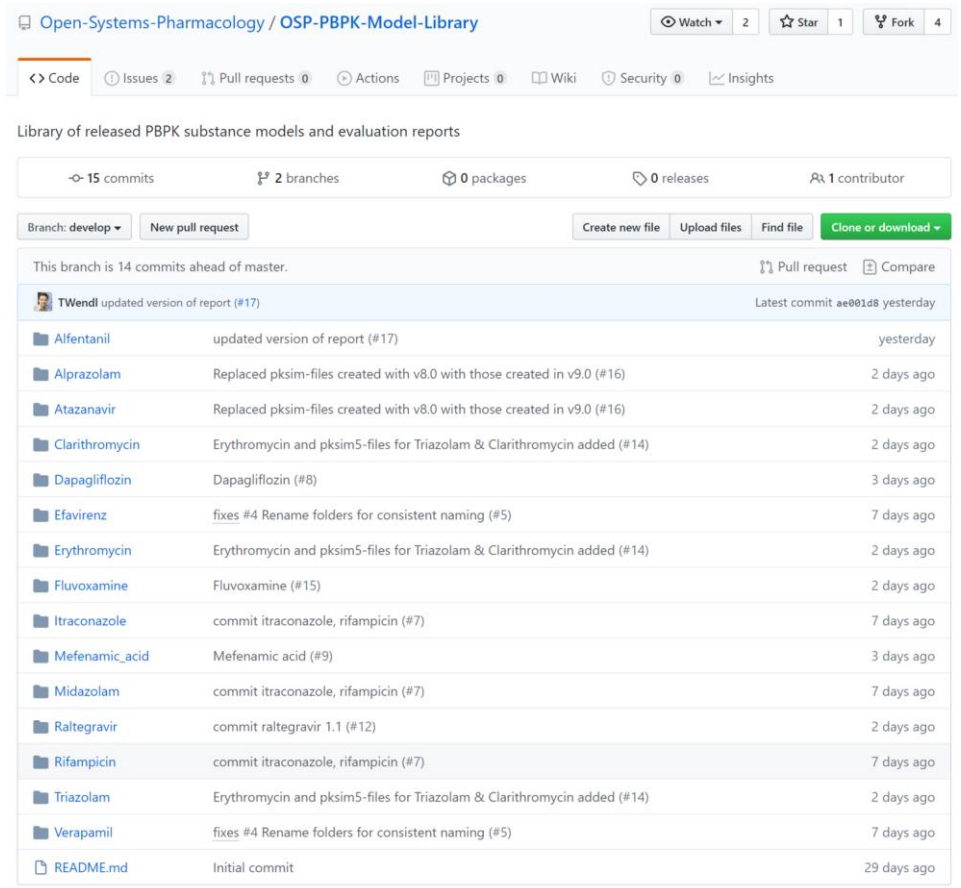
Community-Driven CoU Qualification Framework
Qualification Plans Structure

- **PK-Sim snapshots**
- **Observed data** sets (needed for model development and verification)
- Qualification **scenario description** text modules
- Detailed report **settings** to describe the generation of **charts** and qualification **measures**



Community-Driven CoU Qualification Framework

OSPS Qualified Model Repository



Open-Systems-Pharmacology / OSP-PBPK-Model-Library

Watch 2 | Star 1 | Fork 4

Code | Issues 2 | Pull requests 0 | Actions | Projects 0 | Wiki | Security 0 | Insights

Library of released PBPK substance models and evaluation reports

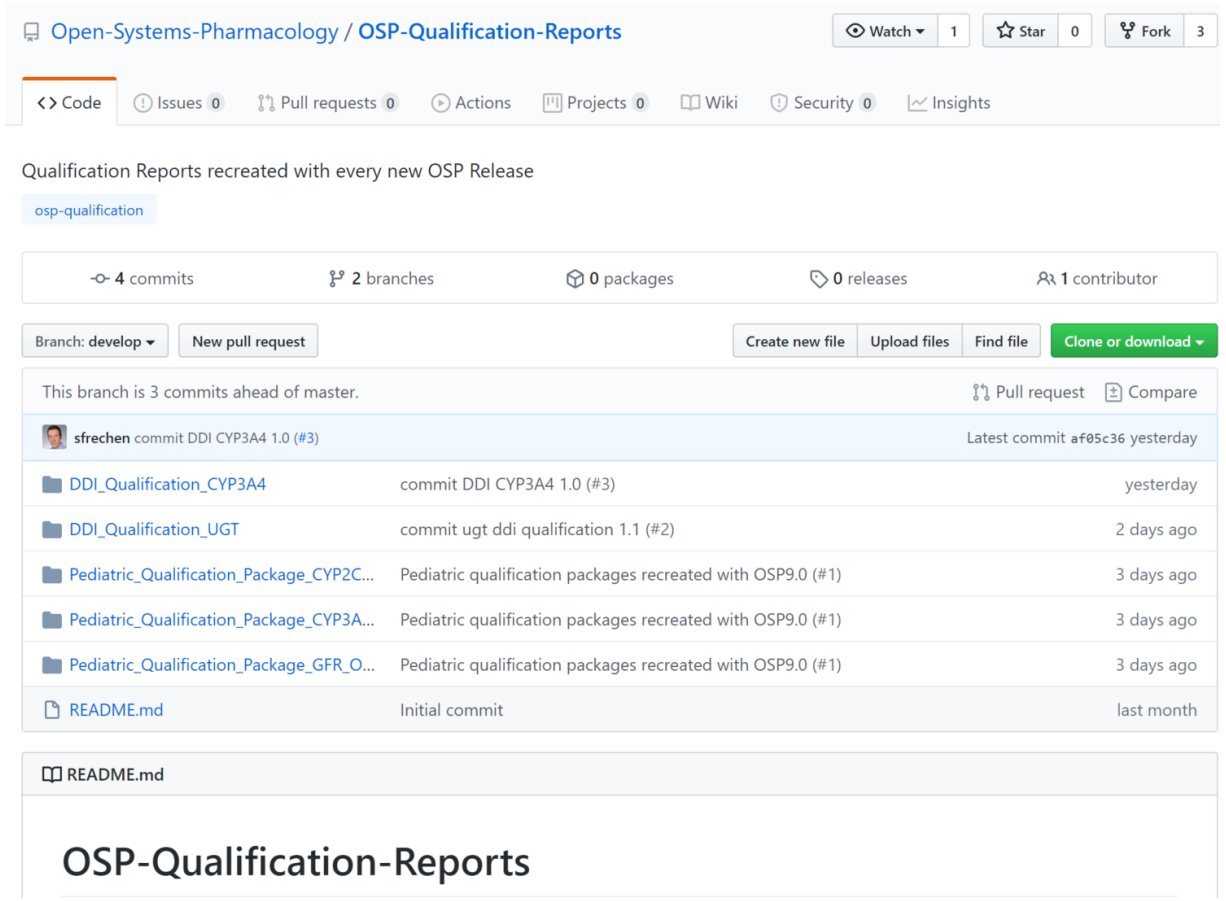
15 commits | 2 branches | 0 packages | 0 releases | 1 contributor

Branch: develop | New pull request | Create new file | Upload files | Find file | Clone or download

This branch is 14 commits ahead of master. | Pull request | Compare

TWendl updated version of report (#17) | Latest commit ae001d8 yesterday

Alfentanil	updated version of report (#17)	yesterday
Alprazolam	Replaced pksim-files created with v8.0 with those created in v9.0 (#16)	2 days ago
Atazanavir	Replaced pksim-files created with v8.0 with those created in v9.0 (#16)	2 days ago
Clarithromycin	Erythromycin and pksim5-files for Triazolam & Clarithromycin added (#14)	2 days ago
Dapagliflozin	Dapagliflozin (#8)	3 days ago
Efavirenz	fixes #4 Rename folders for consistent naming (#5)	7 days ago
Erythromycin	Erythromycin and pksim5-files for Triazolam & Clarithromycin added (#14)	2 days ago
Fluvoxamine	Fluvoxamine (#15)	2 days ago
Itraconazole	commit itraconazole, rifampicin (#7)	7 days ago
Mefenamic_acid	Mefenamic acid (#9)	3 days ago
Midazolam	commit itraconazole, rifampicin (#7)	7 days ago
Raltegravir	commit raltegravir 1.1 (#12)	2 days ago
Rifampicin	commit itraconazole, rifampicin (#7)	7 days ago
Triazolam	Erythromycin and pksim5-files for Triazolam & Clarithromycin added (#14)	2 days ago
Verapamil	fixes #4 Rename folders for consistent naming (#5)	7 days ago
README.md	Initial commit	29 days ago



Open-Systems-Pharmacology / OSP-Qualification-Reports

Watch 1 | Star 0 | Fork 3

Code | Issues 0 | Pull requests 0 | Actions | Projects 0 | Wiki | Security 0 | Insights

Qualification Reports recreated with every new OSP Release

osp-qualification

4 commits | 2 branches | 0 packages | 0 releases | 1 contributor

Branch: develop | New pull request | Create new file | Upload files | Find file | Clone or download

This branch is 3 commits ahead of master. | Pull request | Compare

sfrechen commit DDI CYP3A4 1.0 (#3) | Latest commit af05c36 yesterday

DDI_Qualification_CYP3A4	commit DDI CYP3A4 1.0 (#3)	yesterday
DDI_Qualification_UGT	commit ugt ddi qualification 1.1 (#2)	2 days ago
Pediatric_Qualification_Package_CYP2C...	Pediatric qualification packages recreated with OSP9.0 (#1)	3 days ago
Pediatric_Qualification_Package_CYP3A...	Pediatric qualification packages recreated with OSP9.0 (#1)	3 days ago
Pediatric_Qualification_Package_GFR_O...	Pediatric qualification packages recreated with OSP9.0 (#1)	3 days ago
README.md	Initial commit	last month

README.md

OSP-Qualification-Reports

Installation Verification

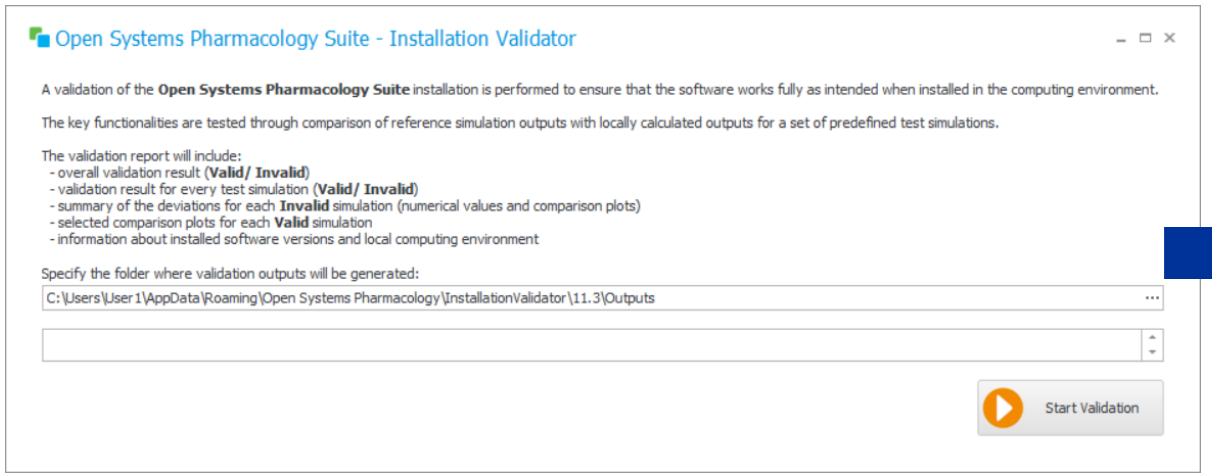
- Installation validation on a target system is ensured by the **fully automated** Installation Validator tool installed as part of the OSP Suite.

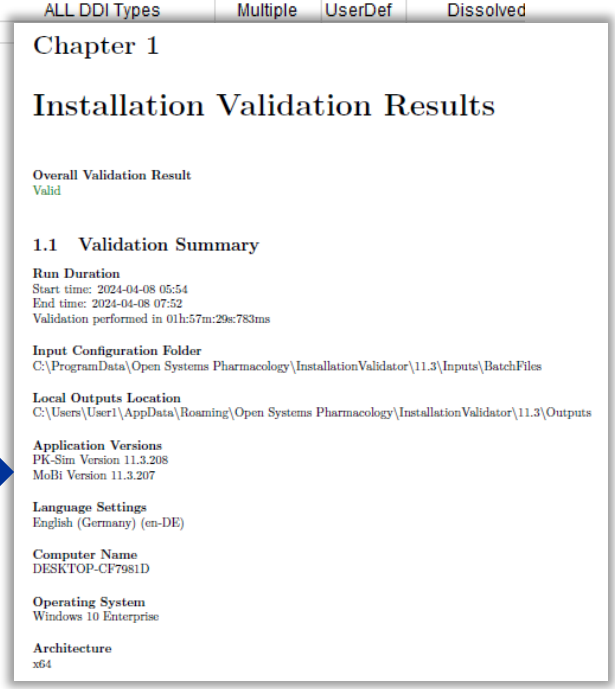
➢ A set of predefined (PBPK) models is being created and simulated in a target modeling environment.

File	Modell	Simulations		Individual							Compound					Application		
		155	Params	Population	Gender	Age	Aging	Enzymes	Transp.	Bind.	Type	pKa	Partition	Permeab.	Process	Dosing	Type	Formulation
Beagle_SingleORAL_Dissolved	4Comp	3	fu/MW/Lipo	Beagle	---	---	---	---	---	---	small	Acid	RR	Standard		Single	Oral	Dissolved
DDI_MultipleCombinations	4Comp	23	---	ICRP_2002	MALE	30	---	Multiple	Multiple	---	small	Multiple	Multiple	Multiple	1st Order/MM Metab. 1st Order/MM Transports ALL DDI Types	Single / Multiple	Oral / IV / UserDef	Dissolved
Dog_MultiORAL_12_12_Dissolved	4Comp	1	---	Dog	---	---	---	---	---	---	small	Acid	RR	Standard				

➢ Simulation results are compared to the *reference simulation results* (reference simulation results are created and validated during the OSP Release validation).

➢ A **validation report** is generated for the target environment.




Chapter 1

Installation Validation Results

Overall Validation Result
Valid

1.1 Validation Summary

Run Duration
Start time: 2024-04-08 05:54
End time: 2024-04-08 07:52
Validation performed in 01h:57m:29s:783ms

Input Configuration Folder
C:\ProgramData\Open Systems Pharmacology\InstallationValidator\11.3\Inputs\BatchFiles

Local Outputs Location
C:\Users\User1\AppData\Roaming\Open Systems Pharmacology\InstallationValidator\11.3\Outputs

Application Versions
PK-Sim Version 11.3.208
MoBi Version 11.3.207

Language Settings
English (Germany) (en-DE)

Computer Name
DESKTOP-CF7981D

Operating System
Windows 10 Enterprise

Architecture
x64

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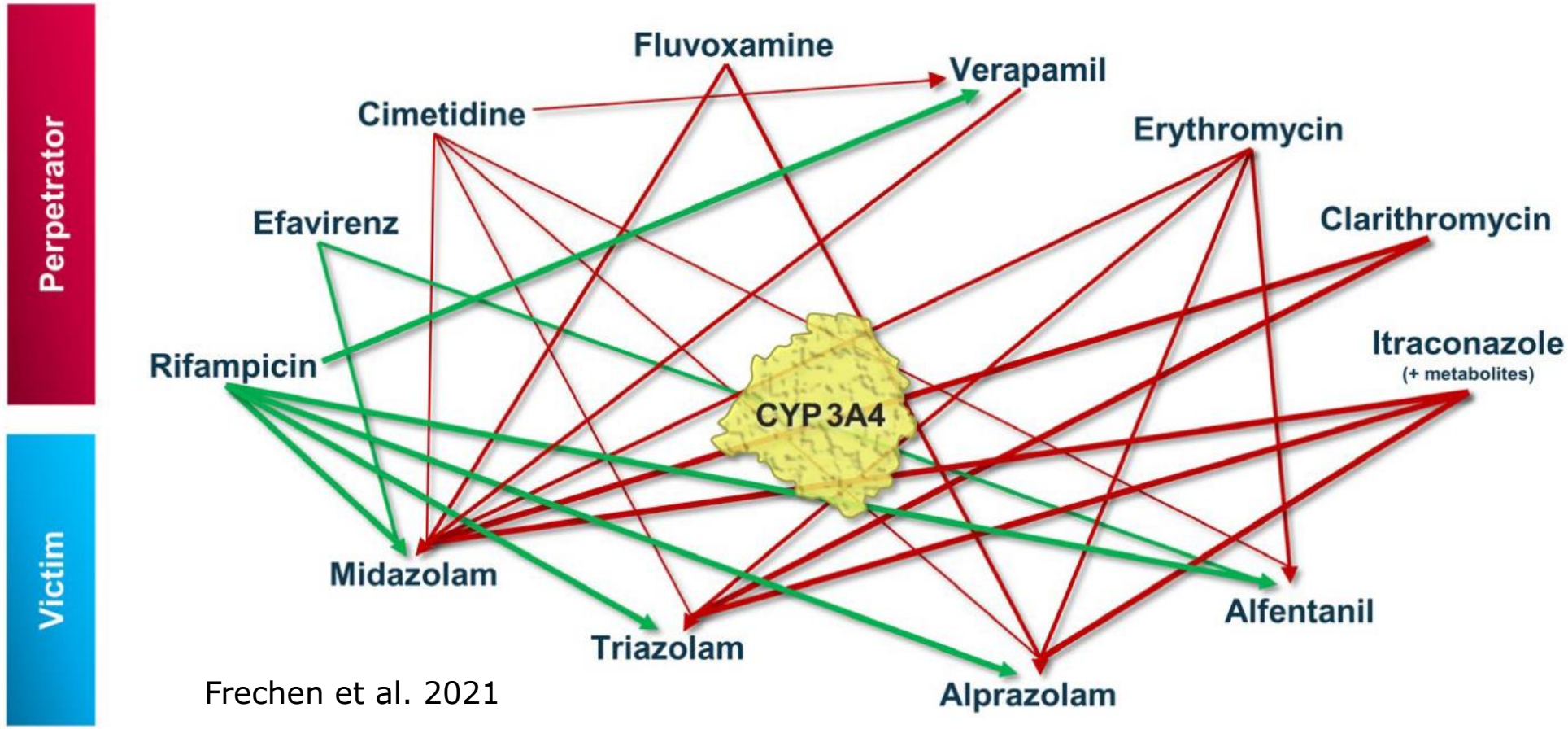
CoU Qualification in Action: Examples

DDI, pediatrics, special populations - aligned with EMA/FDA frameworks

Community-Driven CoU Qualification Framework
Example: CYP3A4 DDI qualification package

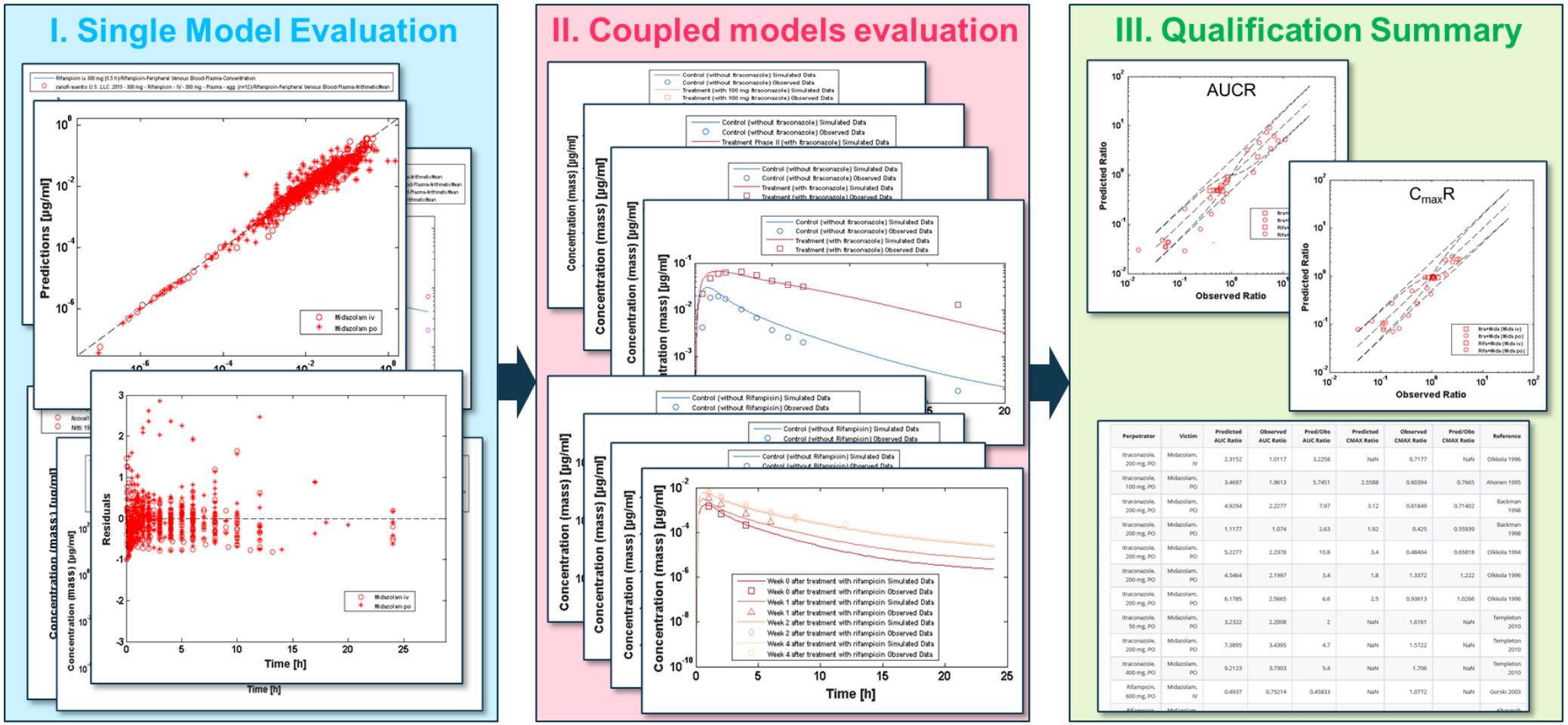
- A **complex network** of index compounds ranging from strong **induction** to strong **inhibition**



Frechen et al. 2021

Community-Driven CoU Qualification Framework

Example: CYP3A4 DDI qualification package



Perpetrator	Victim	Predicted AUC Ratio	Observed AUC Ratio	Pred/Obs AUC Ratio	Predicted CMAX Ratio	Observed CMAX Ratio	Pred/Obs CMAX Ratio	Reference
Itraconazole, 200 mg, PO	Midazolam, IV	2.3152	1.0117	3.2258	NaN	0.7177	NaN	Olkkola 1996
Itraconazole, 100 mg, PO	Midazolam, PO	3.4697	1.9613	5.7451	2.5588	0.60394	0.7665	Ahonen 1995
Itraconazole, 200 mg, PO	Midazolam, PO	4.9294	2.2277	7.97	3.12	0.61849	0.71402	Backman 1998
Itraconazole, 200 mg, PO	Midazolam, PO	1.1177	1.074	2.63	1.92	0.425	0.55939	Backman 1998
Itraconazole, 200 mg, PO	Midazolam, PO	5.2277	2.2378	10.8	3.4	0.48404	0.65818	Olkkola 1994
Itraconazole, 200 mg, PO	Midazolam, PO	4.5464	2.1997	3.4	1.8	1.3372	1.222	Olkkola 1996
Itraconazole, 200 mg, PO	Midazolam, PO	6.1785	2.5665	6.6	2.5	0.93613	1.0266	Olkkola 1996
Itraconazole, 50 mg, PO	Midazolam, PO	3.2322	2.2008	2	NaN	1.6161	NaN	Templeton 2010
Itraconazole, 200 mg, PO	Midazolam, PO	7.3895	3.4395	4.7	NaN	1.5722	NaN	Templeton 2010
Itraconazole, 400 mg, PO	Midazolam, PO	9.2123	3.7303	5.4	NaN	1.706	NaN	Templeton 2010
Rifampicin, 600 mg, PO	Midazolam, IV	0.4937	0.75214	0.45833	NaN	1.0772	NaN	Gorski 2003

Case Study - Successful Regulatory Application

Finerenone PBPK DDI prediction informs US FDA label

The finerenone model validated using clinical data with moderate CYP3A inhibitors

The Division of Pharmacometrics has reviewed the PBPK reports, supporting modeling files, and the Applicant's responses to the FDA's information requests (IRs) submitted on January 28 and March 17, 2021, and concluded the following:

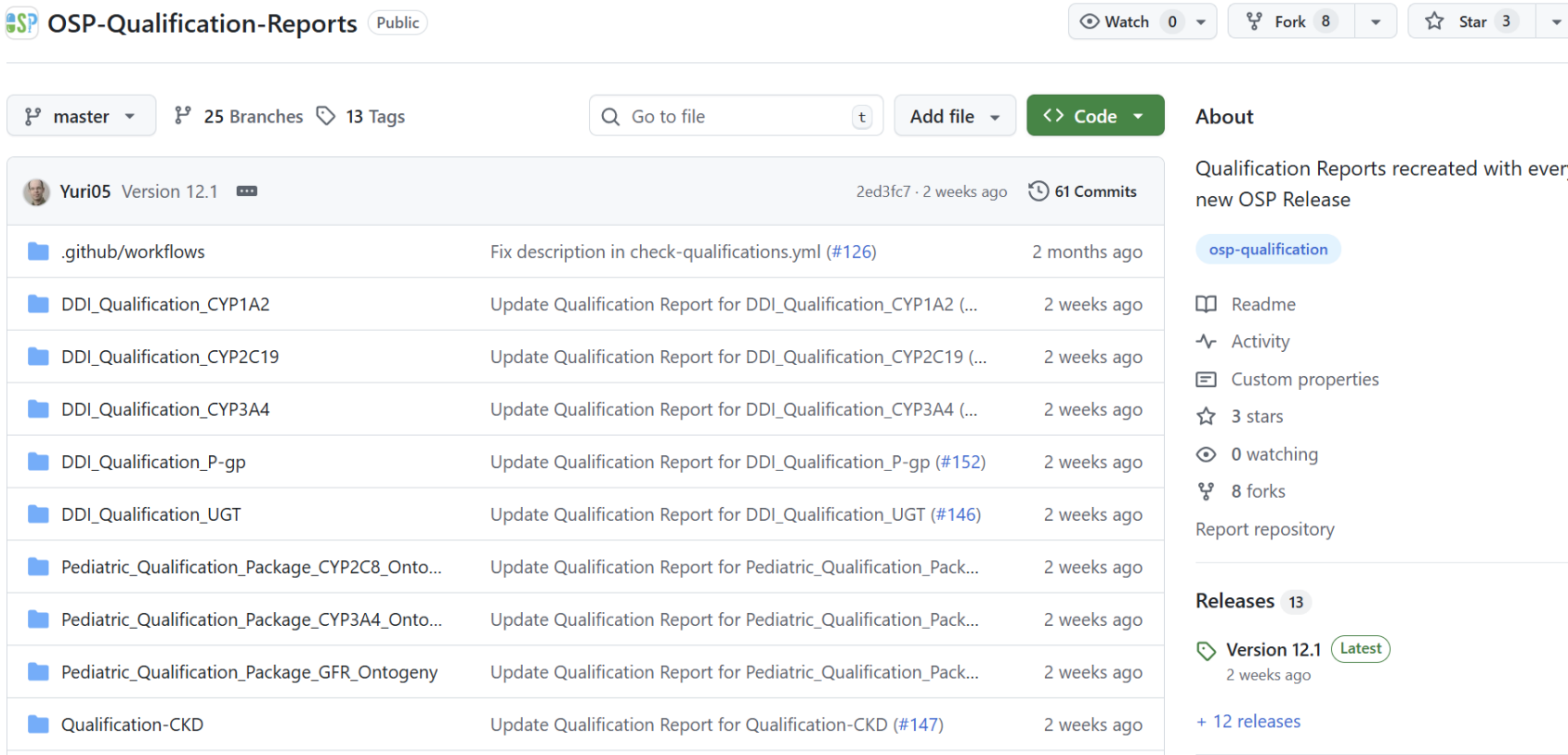
- The finerenone model is adequate to predict the finerenone PK profiles following a single 1 hour intravenous infusion (0.25, 0.5 or 1 mg), a single oral dose administration (1.25, 2.5, 5, 7.5 or 10 mg), or multiple oral dose administration (10 mg BID, 20 mg BID, and 40 mg QD) in healthy subjects.
- The finerenone model is adequate to predict the effect of itraconazole or clarithromycin on finerenone PK following a single oral dose administration of finerenone (10 mg) and multiple dose administration of itraconazole (200 mg BID) or clarithromycin (500 mg BID) in healthy subjects. Model predicted finerenone geometric mean AUC ratio was higher than 5 and 3.5, when co-administered with itraconazole and clarithromycin, respectively, in healthy subjects.
- The finerenone model is adequate to predict the effect of fluvoxamine on finerenone PK following a single oral dose administration of finerenone (10 mg) and multiple dose administration of fluvoxamine (100 mg BID) in healthy subjects. Model predicted finerenone geometric mean AUC ratio was approximately 1.55 when co-administered with fluvoxamine in healthy subjects.
- The finerenone model is adequate to predict the effect of efavirenz on finerenone PK following a single oral dose administration of finerenone (10 mg) and a single dose or multiple dose administration of efavirenz in healthy subjects. Model predicted finerenone geometric mean AUC ratio was approximately 0.2, 0.2, and 0.6, when co-administered with 400 mg QD, 600 mg QD or 400 mg single dose of efavirenz, respectively, in healthy subjects.
- The finerenone model is adequate to predict the effect of rifampicin on finerenone PK following a single oral dose administration of finerenone (10 mg) and multiple dose administration of rifampicin (600 mg QD) in healthy subjects. Model predicted finerenone geometric mean AUC ratio was approximately 0.07 when co-administered with rifampicin in healthy subjects.
- Model extrapolation of clinical study results with moderate inhibitors to the studies with strong modulators may result in uncertainties regarding the predicted exposure change with strong modulators.

Taken from:
FDA - CENTER FOR DRUG EVALUATION AND RESEARCH
"Integrated Review"
https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=overview.process&ApplNo=215341

→PBPK Review
p. 202 - 211

Addressing EMA Qualification Requirements

- **Direct alignment with EMA qualification requirements:**
  - Platform Qualification and Validation ✓
  - External evidence benchmarking and Model Evaluations ✓
  - Clearly defined processes for development and qualification/validation ✓
  - Version control & lifecycle ✓

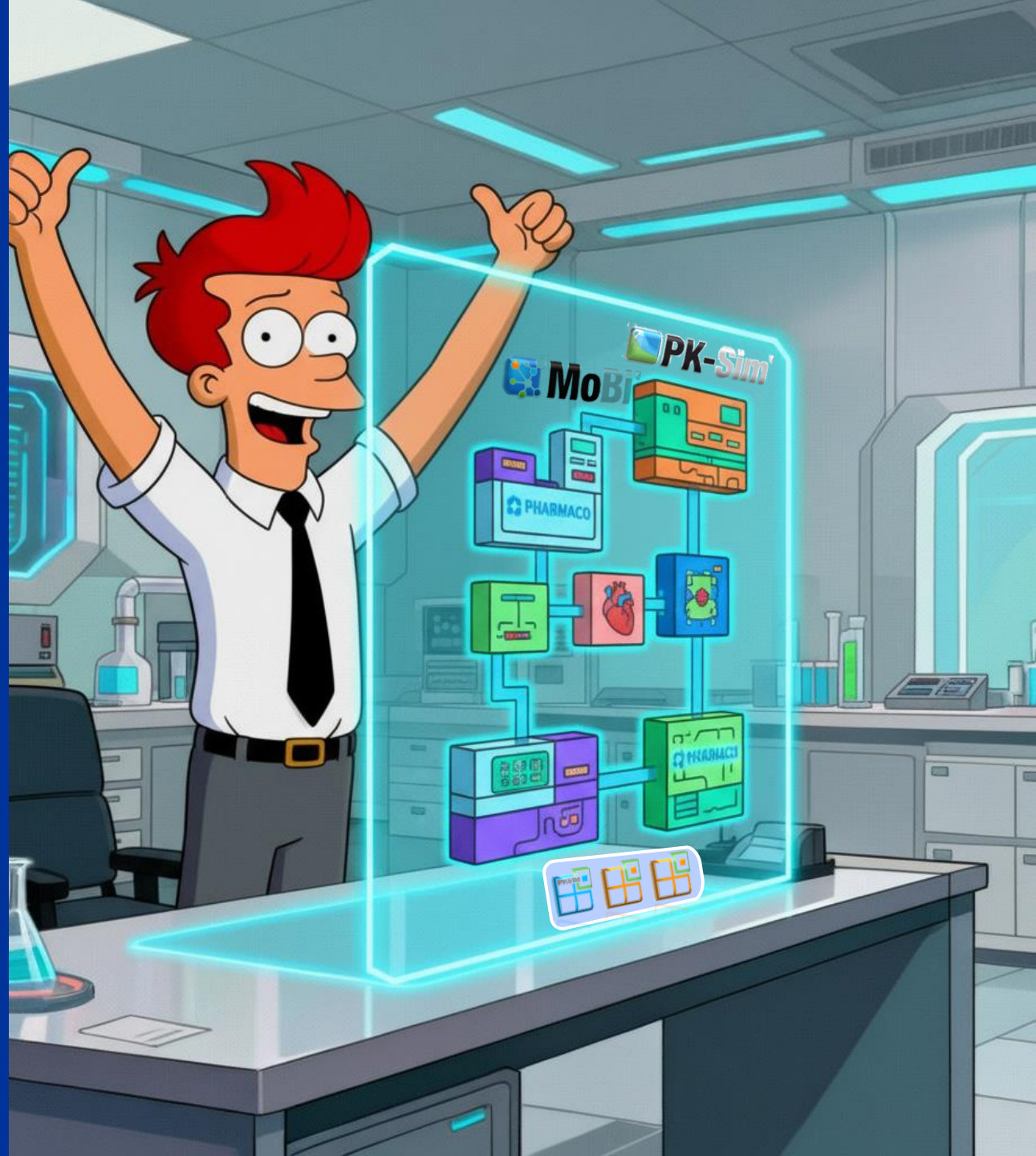


EMA
EUROPEAN MEDICINES AGENCY

HMA
Heads of Medicines Agencies

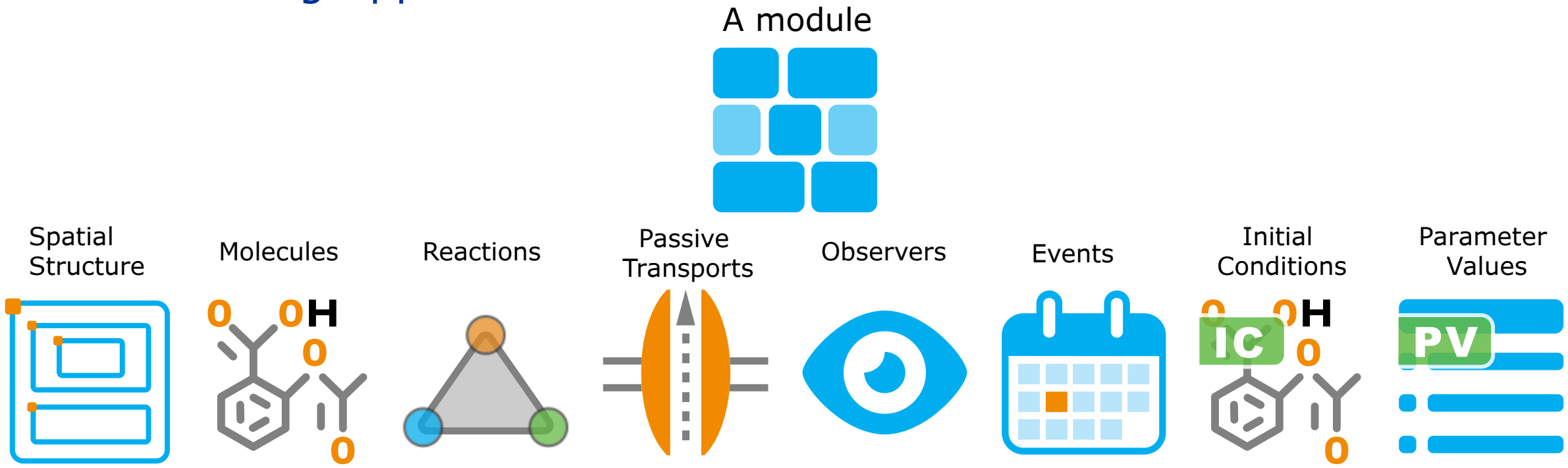
Beyond PBPK: The Modular MIDD Future

Expanding to PBPK-QSP integration and qualification for complex translational models



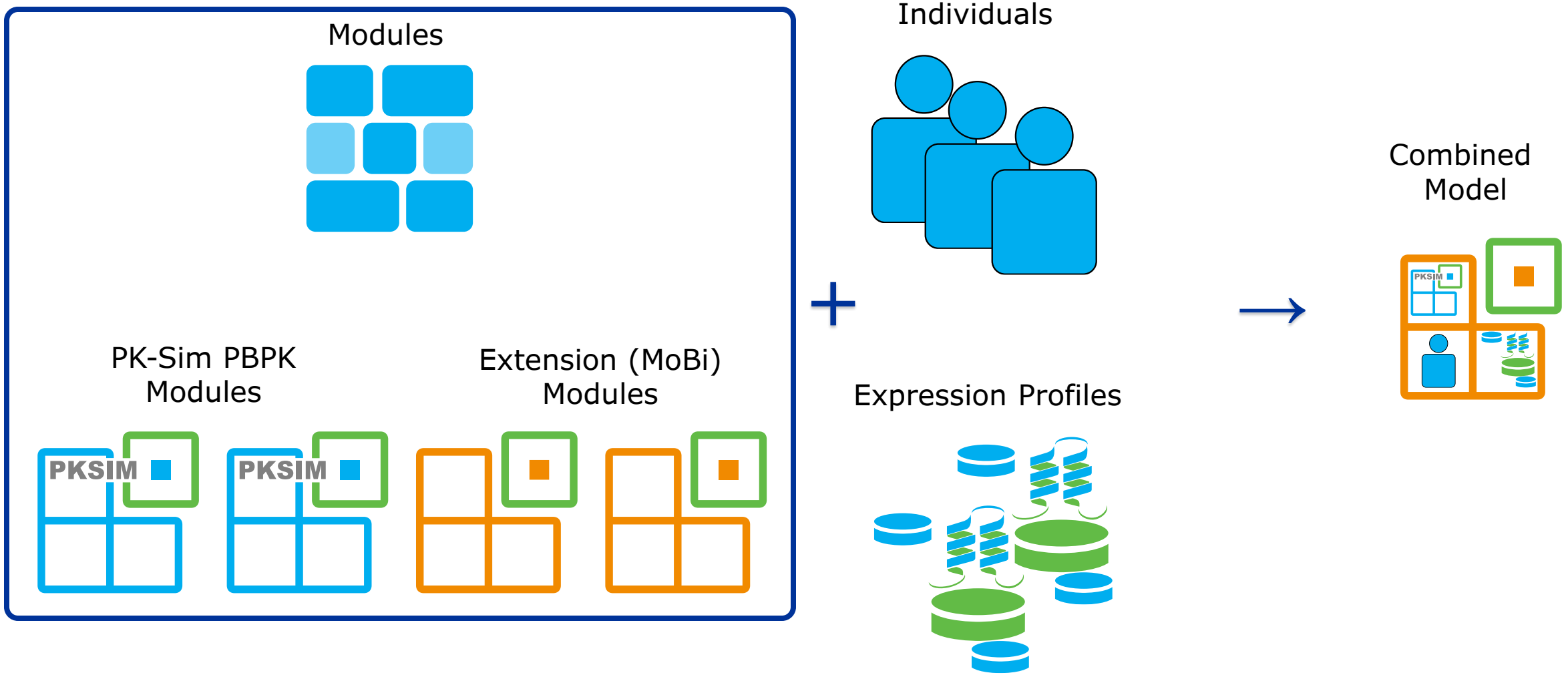
Modular M&S Concept of OSP V12+

Model Building Approach



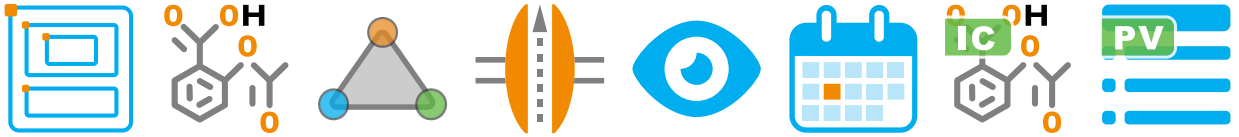
→ This is the “FULL” breadth of **components** from the **PK-Sim whole-body PBPK models**

Modular M&S Concept of OSP V12+
Model Building Approach

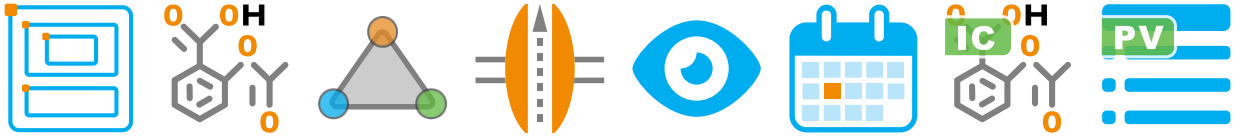


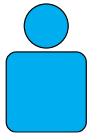
Modular M&S Concept of OSP V12+
Model Building Approach

CompoundA

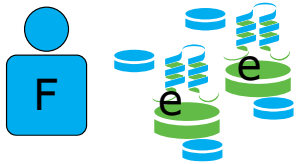


CompoundB

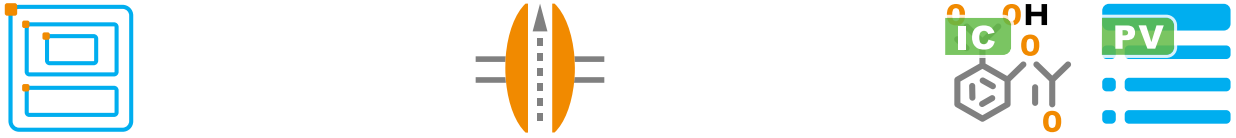




31 years old female
Extensive metabolizer



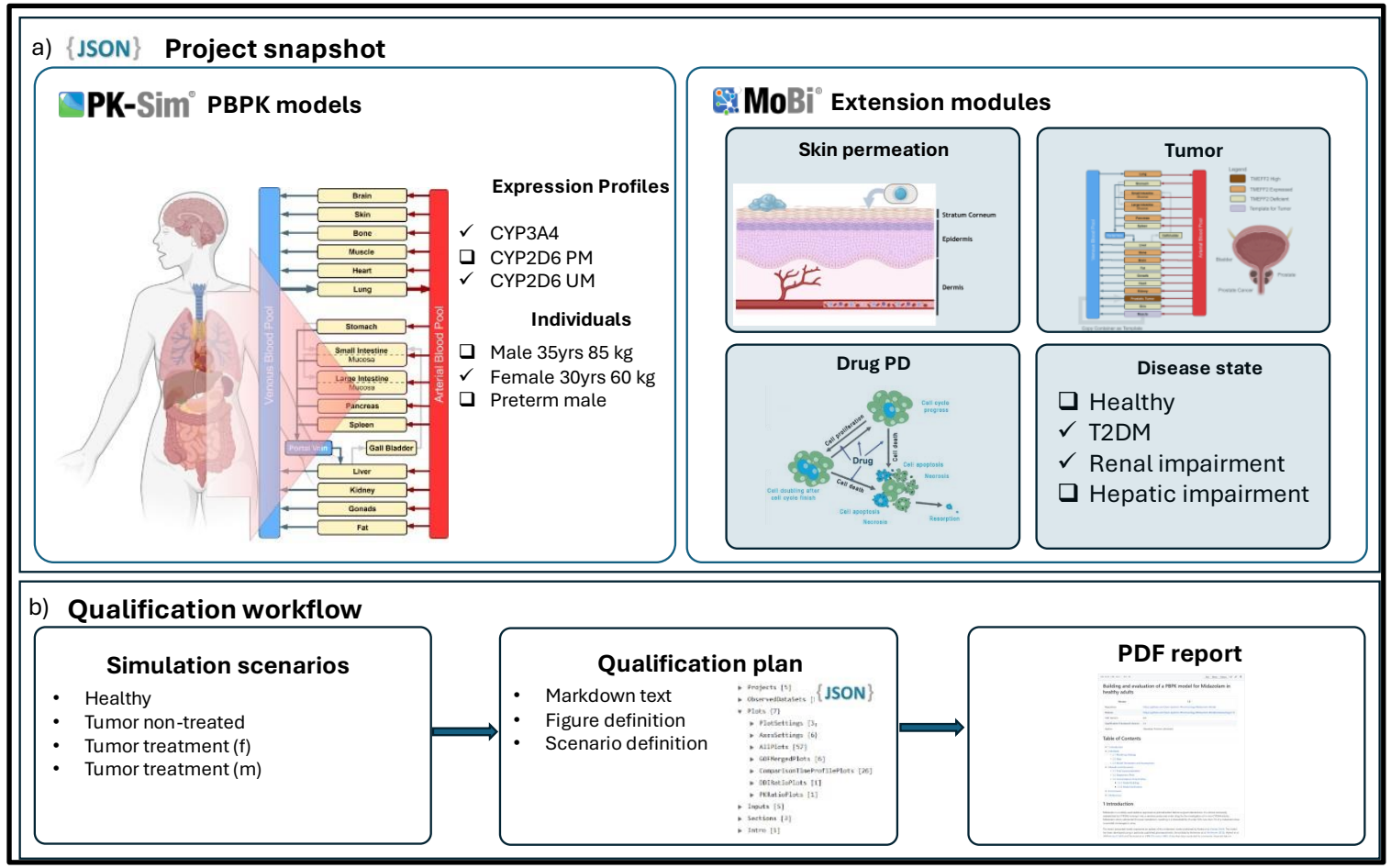
Pregnancy



CompoundA effect model
Disease population

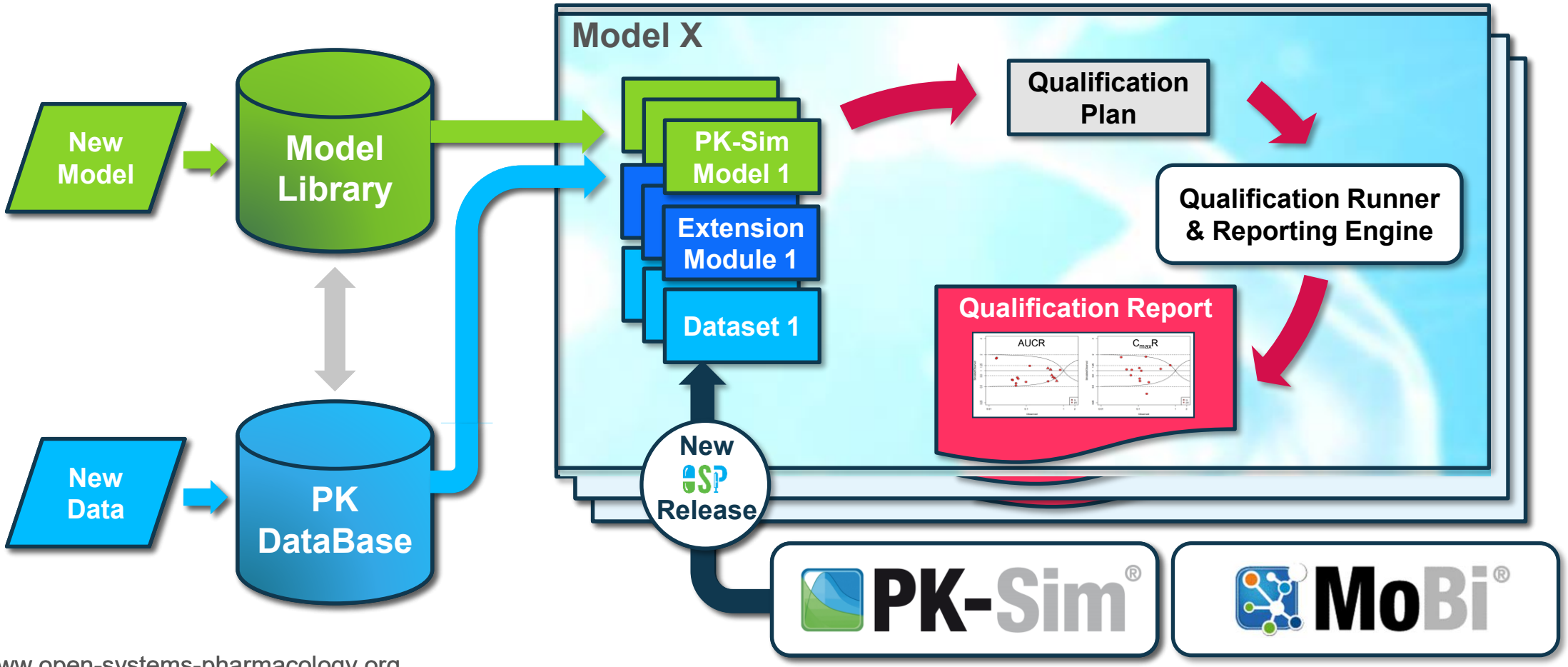
PBPK-QSP Platform Qualification
"Expanded" MoBi Project Snapshot

- 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



PBPK-QSP Platform Qualification

"Expanded" Qualification Plan and Routine



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Modular MIDD Ecosystem

Beyond PBPK to PBPK-QSP

Discovery,
Toxicology,
Translational,
Clinical teams

quarto

Reporting Framework

Development Lifecycle

Discovery, HTS, chem/bio-informatics data

AI/ML

PBPK-QST Modelling & Qualification & Reporting

Clinical trial analysis

(Pre)Clinical data

PBPK model library

GitHub

PBPK Lifecycle

PBPK Model

PK-Sim®

Extension Modules

MoBi®

QST Lifecycle

QST model library

GitHub

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Take-Aways

OSP = Equitable high-quality Solutions for Mechanistic Model Development and Qualification

Community Impact & Adoption

- OSP Community Conference (~105+ Participants yearly)
- Online Training Platform (ESQlabs, ~200+ subscribers)
- Workshops by CROs (ESQlabs, Pharmetheus, BioNotus, …)
- ~ 500+ Peer Reviewed Publications up to 2024 (+ 100 and increasing per year
- **Regulatory Submissions**:

Drug name	Company	Indication	Link	Software
Vesicare LS (Solifenacin)	Astellas	Neurogenic detrusor overactivity (NDO)	https://www.accessdata.fda.gov/drugsatfda_docs/nda/2020/209529Orig1s000ClinPharmR.pdf	PK-Sim® v5.1
Kerendia (Finerenone)	Bayer	Chronic kidney disease (CKD)	https://www.accessdata.fda.gov/drugsatfda_docs/nda/2021/215341Orig1s000IntegratedR.pdf	PK-Sim V7.4 and 9.1
Verquvo (Vericiguat)	MSD	Heart failure (HF)	https://www.accessdata.fda.gov/drugsatfda_docs/nda/2021/214377Orig1s000IntegratedR.pdf	PK-Sim V7.1 and MoBi V7.1

Conclusions

Key takeaways:

- Open source ≠ lower quality,
  but = higher **quality** if community-backed
- Transparency builds **trust**
- Community approach enables
  content creation and transparent **qualification**
- Framework ready for **regulatory use**

Acknowledgements

- **OSP Management Team members**
  - Acknowledging the Specific Contributions of
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  - (EU, Gates Foundation, BMBF (Germany), EFSA (EU), NC3R (UK), CIR (France), …)
- **Community contributors**

(And many more…)

Thank you

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