Development of an end-to-end Quantitative Model-Informed Drug Development (MIDD) ECOSYSTEM

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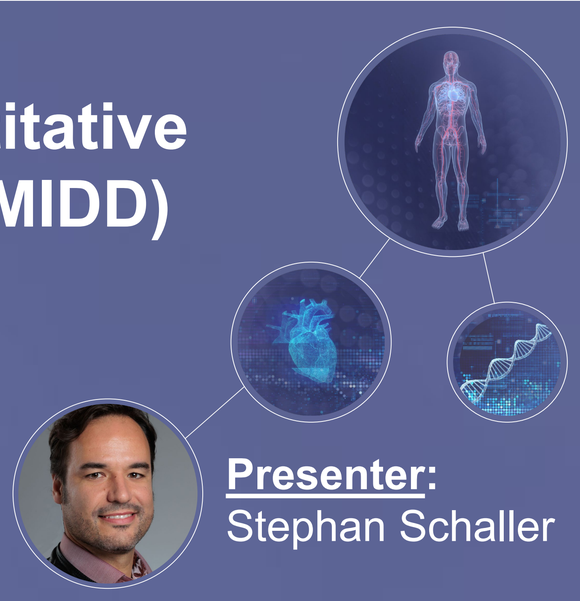

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Background

Model-Informed Drug Development (MIDD) is essential in pharmaceutical R&D. Growing therapeutic complexity and regulatory expectations for model qualification **necessitate a structured, automated, and scalable MIDD ecosystem**.
The Open Systems Pharmacology (OSP) Suite [1] Version 12 introduces **modularization capabilities** enabling such an integrated ecosystem. This supports seamless **development, validation, and deployment** of Physiologically Based Pharmacokinetic (**PBPK**) and Quantitative Systems Pharmacology/Toxicology (**QSP/T**) models, ensuring **robust**, **reproducible decision-making**.
It was initially conceived to enhance PBPK-QSP platform management for the Diabetes Disease Platform [2, 3].

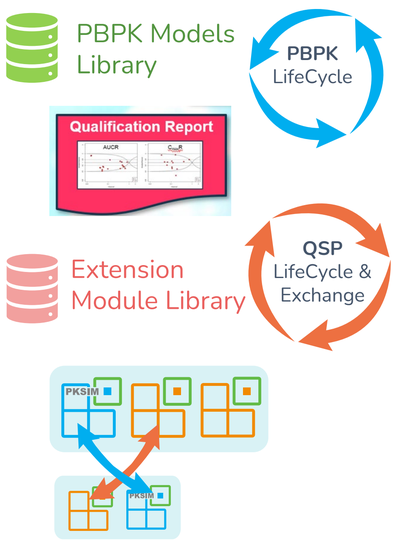
Results

The **end-to-end MIDD ecosystem**, leveraging OSP Suite V12, implements structured **model storage, validation, modularization, and continuous integration**. Key components include:

- A continuously expanding **PK-Sim model library** of qualified PBPK models. This centralized repository provides **verified models** for various drugs, populations (e.g., pediatric, disease-states), and mechanistic scenarios, **reducing duplication and standardizing methodologies**. Automated model **qualification** ensures reliability for applications like drug-drug interaction (DDI) assessments and special population extrapolations.

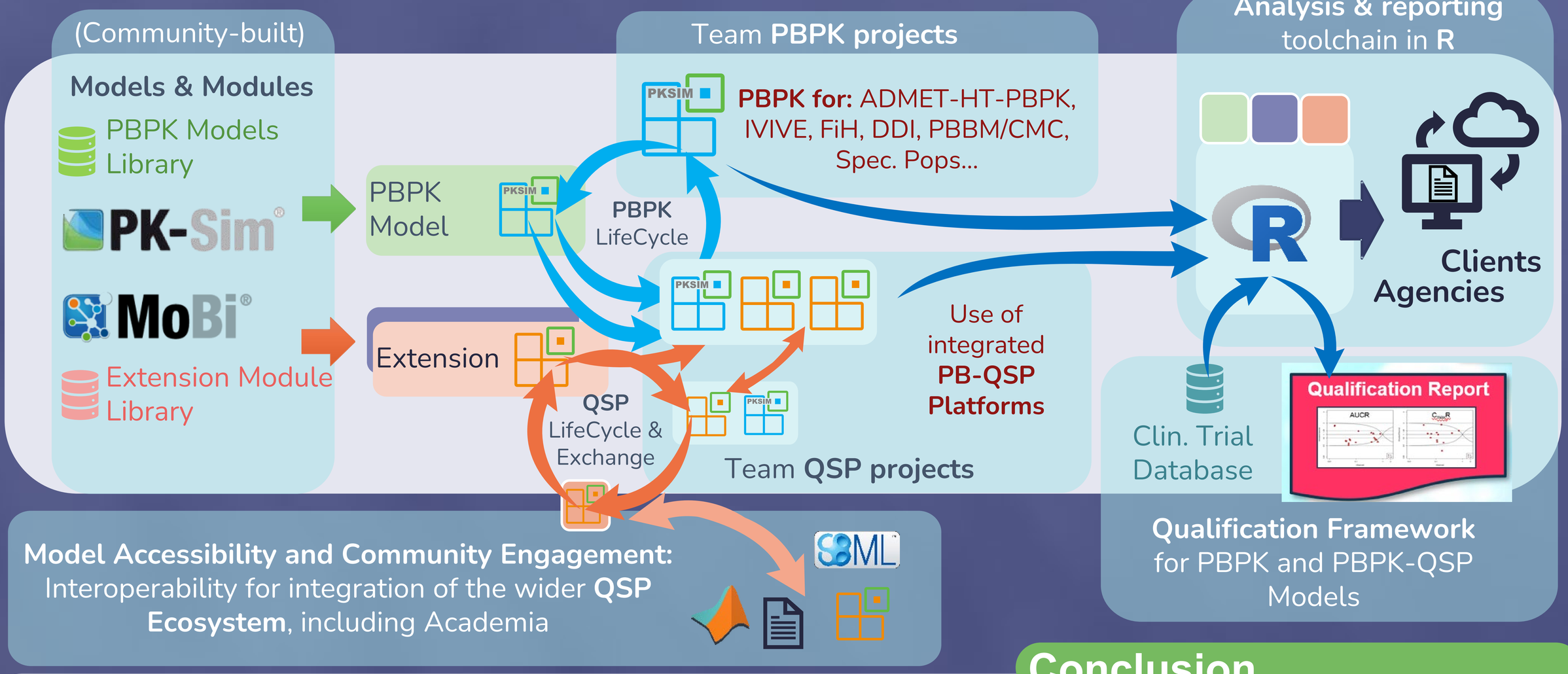
- A **MoBi module library** of community-driven QSP/T models, encapsulating disease biology and drug mechanisms. It offers **prebuilt, validated modules for disease progression and pharmacodynamic effects**, enabling pathway-based **PBPK-QSP integration**. This fosters **open-source collaboration, model sharing, and version control**, efficiency.

- **Modular interchangeability** of PBPK models within QSP platforms, a key OSP Suite V12 innovation, enabling Continuous Integration/Continuous Deployment (CI/CD). This **allows dynamic PBPK model replacement in QSP frameworks and automated PBPK-QSP platform qualification** against predefined criteria, ensuring models remain current and continuously validated for regulatory compliance.



This integrated approach, bridging PBPK and QSP/T modeling, has been successfully implemented across diverse pipelines, including **in-vitro systems**, **high-throughput PBPK**, custom modules (e.g., **ocular absorption, pregnancy**), **and integrated disease/drug effect models across safety endpoints and therapeutic areas**.

Figure 1: Modeling & simulation workflow in PBPK-based pediatric evaluations [4] (Figure is courtesy of www.open-systems-pharmacology.org)



Conclusion

The **end-to-end MIDD ecosystem**, powered by OSP Suite V12, represents a significant **advancement in PBPK-QSP** modeling, effectively linking model development, qualification, and regulatory delivery. Its core strengths—continuously evolving PK-Sim and MoBi libraries for reusable, validated models, coupled with modular interchangeability and CI/CD for agile, automated PBPK-QSP platform qualification—drive this transformation. By implementing automated qualification, standardized repositories, and modular workflows integrated with OSP-R and ESQlabs-R packages, the **ecosystem markedly enhances transparency, reproducibility, and regulatory credibility**. This ultimately empowers regulatory engagement with robust, continuously validated models, accelerating drug development, reducing predictive uncertainty, and supporting evidence-based approvals. The **synergy of open-source software, modularity, and automation is pivotal for maximizing MIDD's impact in pharmaceutical R&D**.

References

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Modeling

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