OPEN SYSTEMS PHARMACOLOGY

PBPK modeling for locally acting drug products
- MoBi and R-Toolbox -

Session 4, PK-Sim/MoBi FDA Workshop
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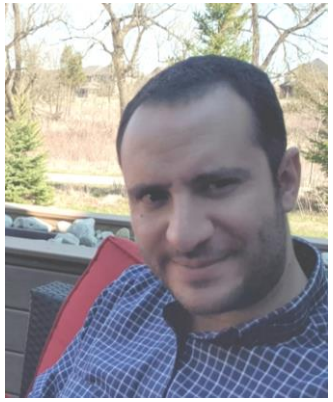

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Session 4 Agenda

Welcome and Introduction to Open Systems Pharmacology (OSP)

1. Introduction to MoBi and how it is linked to PK-Sim and R
2. Showcase – Model building – MoBI

Break

Presentation of PBPK modeling of locally acting drugs using the OSP platform

1. Pulmonary drug delivery
   i. Showcase: Integration of R
   ii. Showcase: MoBi and PK-Sim interaction

Break

2. Dermal drug delivery

Wrap-up of Session 4 and the Workshop Series

Open Systems Pharmacology

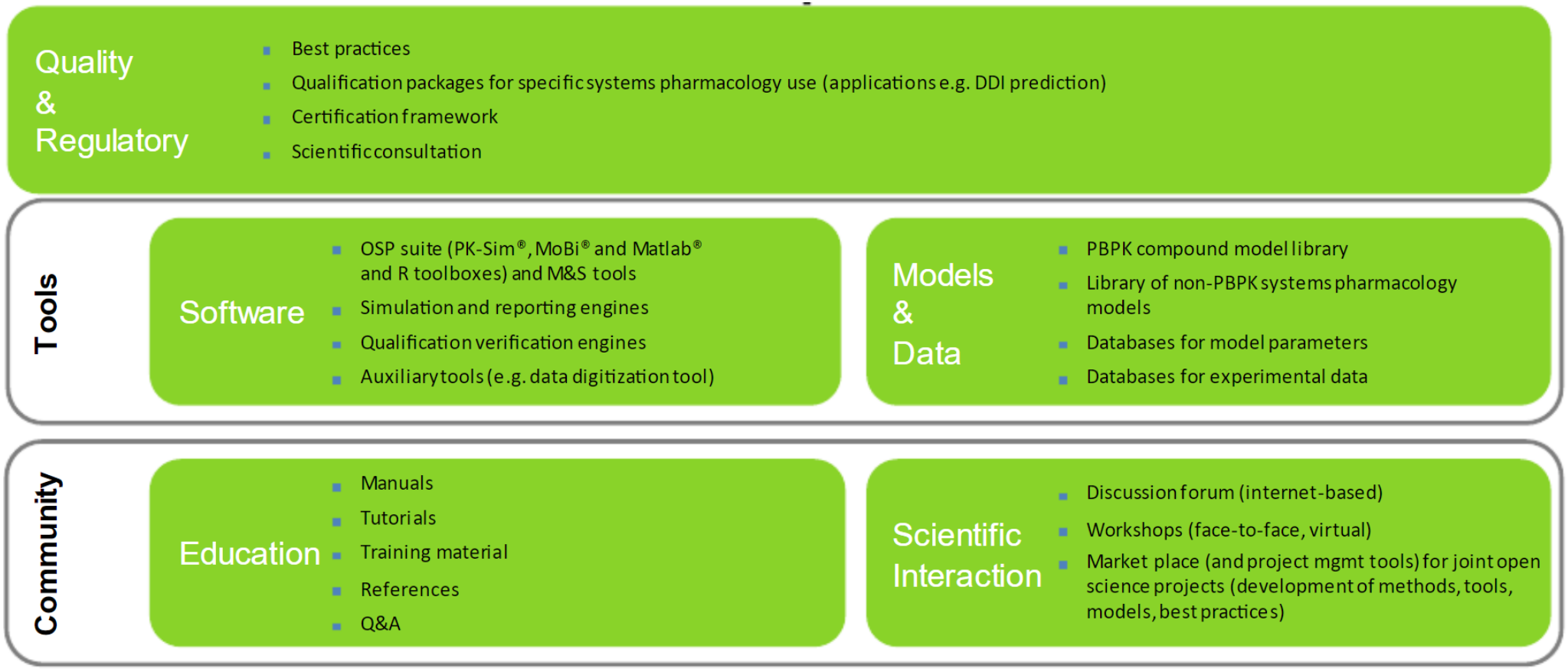
Vision

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 scope of OSP addresses high priority applications of Systems Pharmacology and the need to continuously develop the scientific, methodological and regulatory foundation together with the software platform



OSP Management Team coordinates the interplay of focus areas and interfaces between them. Dedicated Focus Groups conceptualize, design and progress the individual areas.

OSP Management Team organize coordination and oversee all activities (bi-weekly meetings)

- Rolf Burghaus, Bayer AG
- Andrea Edginton, University of Waterloo
- Valvanera Vozmediano Esteban, University of Florida
- Andreas Kovar, Sanofi
- Thorsten Lehr, Universität des Saarlandes
- Jörg Lippert, Bayer AG
- José David Gómez Mantilla, Boehringer Ingelheim
- Matthew M. Riggs, Metrum Research Group
- Stephan Schaller (Chair), esqLABS
- Michael Sevestre, Design2Code
- Erik Sjögren, Pharmetheus, Uppsala University
- Juri Solodenko, Bayer AG
- Alexander Staab, Boehringer Ingelheim
- Donato Teutonico, Sanofi

OSP Sounding Board provides scientific/technical consultancy to MT and informs on trends (yearly meeting with MT)

- Sebastian Frechen, Bayer AG
- Mats Karlsson, Uppsala University
- Peter Milligan, Pharmetheus
- Jan Schlender, Bayer AG

Focus groups are expected to conceptualize and coordinate activities of the respective field.
Includes a OSP MT sponsor, a chair and OSP community members.

Current Focus Groups (1/2)

Focus Group	Objective	Lead (GitHub UserID)
Absorption	The addition of model structures defining additional routes of administration/absorption is required to expand the application scope of the software in a consistent manner across users. The overall objectives are to define processes for 1. Technical generation of new routes of absorption destined for the OSP Suite 2. Evaluation of those absorption modules.	Erik Sjörgren (Erik-Sjogren)
Automation	Automation is a strategic theme of the OSP MT. Automation obviously is a means to increase efficacy but also enables the execution of large technical tasks like population or trials simulations that cannot be conducted manually. Due to its intrinsic transparency, automation is an element of quality by design.	Juri Solodenko (Yuri05)
Community engagement	• To streamline official outside communication channels of OSP – Social Media: LinkedIn / Twitter – Newsletter / OSP News Section – OSP Booth at conferences – OSP Events (Hackathon, …) • Use Communication Channels to increase community engagement • Obtain statements of endorsement • Sustain Community Collaboration Framework	Stephan Schaller (StephanSchaller)
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)

Current Focus Groups (2/2)

Focus Group	Objective	Lead (GitHub UserID)
PBPK best practices	Establishing Standards for PBPK Model Development and Application to Ensure Reliability, Reproducibility and Transparency, Independent of Modeling Platform. The standards should be considered when developing a PBPK model, regardless of the platform. Not a how-to-guide	Matthew Riggs (riggsmm)
PD	• PBPK/PD & QSP modeling is a strategic theme of the OSP MT • Identify needs for enabling / facilitating PD/QSP modelling in PK-Sim and MoBi • To streamline PD efforts of OSP • Derive a strategy for / identify public or industrial collaborations or funding sources to sponsor roadmap implementation	Stephan Schaller (StephanSchaller)
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)
Suite Release Mgmt. / Software Usability	The software suite is a pillar and the nucleus of OSP. Development and maintenance of the suite is a core element of the OSP mission. Active Release Management is required to execute on this mission.	Juri Solodenko (Yuri05)

Managed Open Source

- OSP Suite uses **GitHub** (https://github.com) as a source control platform
- Release planning is realized via the GitHub "Projects" feature. Issues are organized by milestones and effort estimates are proposed and tracked. All of these efforts can be seen by anyone. Release planning and release are only done by the core development team.
- Approved "official" releases of the OSP Suite are published on the GitHub Platform and can be downloaded by any user (no GitHub account is required for this). Full release histories are available.
- Rigorous software development practices uses Continuous Integration (CI) that includes test automation, build automation, code quality analysis and artifact repository. Nightly builds are accessible to anyone and thus always in beta mode for the future version.

OSP Sessions

1. Introduction to PK-Sim
2. PK-Sim applied for modeling of oral drug absorption
3. The Qualification Concept of OSP and its exemplary application to DDI and pediatric predictions with PK-Sim
4. Application of PBPK modeling of locally acting drugs – possibilities and considerations