GMP
Groupe de Métabolisme et Pharmacocinétique

Physiologically based Pharmacokinetic (PBPK) Modeling
4th-6th December 2024 – Faculty of Pharmacy Paris Cité (France)

This 2.5-day workshop is co-organized by the **directors of the Master 2 in PK** (Lyon, Marseille, Paris and Toulouse), **PhinC Development** and the **GMP**.

For registration, ple. **For information**, please contact Laurence Del Frari (laurence.del.frari@pierre-fabre.com)

Workshop overview and objectives

This workshop is designed to provide participants with the necessary information needed for Physiologically Based Pharmacokinetic (PBPK) modeling. New Chemical and Biological Entities will be considered when applicable.

The workshop has been structured into two parts:

- 1 day: four keynote lectures (90 to 120 minutes each) on the main applications of PBPK (including case studies)
- 1.5 day: hands-on exercises.

Agenda

Wednesday 4th (afternoon) & Thursday 5th (morning) December 2024: Keynote lectures

Time	Title	Speakers
Wednesday		
13:30 - 13:35	Welcome	***GMP***
13:35 - 15:05	**Prediction of human pharmacokinetics from preclinical data** • Cross species extrapolation in PBPK • Use of in vitro data to predict Pharmacokinetics • Use of in vitro data to predict Pharmacodynamics	***Donato Teutonico*** *(Sanofi)*
15:05 - 15:30	Coffee break	
15:30 – 17:30	**Biopharmaceutic and Drug-Drug Interaction** • Formulation and solubility • Food effect prediction (including examples) • Drug-Drug Interaction (including examples)	***Letizia Carrara*** *(Servier)*
Thursday		
9:00 - 10: 30	**Specific populations** • Physiological changes in Hepatic and Renal impairment • Impact of severity of disease on changes in pharmacokinetics • Regulatory guidance and current status of organ impairment PBPK models in clinical trial waivers • Pediatric population	***Oliver Hatley (Certara)***

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10:30 - 11:00	Coffee break	
11:00 - 12:30	**PBPK-PD for Biologics** **– Large Molecules and Novel Modalities** • Physiological aspects of large molecule ADME, including biodistribution and FcRn-mediated recycling • Implications on PK of target-mediated drug disposition (TMDD) and integrating PD into PBPK-QSP models • Regulatory guidance and current status of large molecule PBPK modeling	***Stephan Schaller*** *(ESQlabs GmbH)*
12:30 - 13:30	Lunch	

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Thursday 5th (afternoon) and Friday 6th December 2024: Hands-on exercises

<table>
<tr><th>Time</th><th colspan="2">Title</th><th>Facilitators</th></tr>
<tr><td>Thursday</td><td colspan="2"></td><td></td></tr>
<tr><td>13:30 - 17:30*</td><td colspan="2">Building a PBPK model
Case study of hydrocodone (CYP3A4 and CYP2D6 substrate)
Modeling of parent drug and metabolite</td><td rowspan="8">Virginie Gualano
(PhinC)

Corentin Mit
(PhinC)

Laurence Del Frari
(Pierre Fabre)</td></tr>
<tr><td>18:30 - 20:30</td><td colspan="2">Cocktail</td></tr>
<tr><td>Friday</td><td colspan="2"></td></tr>
<tr><td>8:30 – 12:30*</td><td>Subgroup 1
(15 delegates)</td><td>Subgroup 2
(15 delegates)</td></tr>
<tr><td></td><td>DDI applications
Case study with paroxetine, a strong inhibitor of CYP2D6</td><td>First in Human applications
First in Human applications
Modeling animal profiles for human predictions
Optional (Prediction of exposure with different ER tablets/food effect)</td></tr>
<tr><td>12:30 - 13:30</td><td colspan="2">Lunch</td></tr>
<tr><td>13:30 - 17:00*</td><td>Subgroup 1
(15 delegates)</td><td>Subgroup 2
(15 delegates)</td></tr>
<tr><td></td><td>First in Human applications
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* Including a coffee break

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Number of participants

- 20 students registered in one of the 4 Master 2 co-organizing this workshop
- 10 industrial/academic delegates

Registration fees (including lunch, coffee breaks and cocktail)

- Student rate: free registration
- Industrial/academic rate: 850 € (+ 50 € for GMP membership)

Location

- Faculty of Pharmacy Paris Cité - site de l'Observatoire de Paris

Software

- The different softwares used in PBPK will be presented (GastroPlus®, MC Sim, PK-SIM®, and SimCYP®).
- The hands-on exercises will be performed with GastroPlus®

Requirements

Delegates are required to bring a laptop computer and will be provided with free access to GastroPlus® for the duration of the workshop. No prior experience with GastroPlus® is required. However, delegates will be invited to follow tutorials for a faster handling of the software.

Speaker Biography

Donato Teutonico (PharmD, PhD - Sanofi)

Donato Teutonico has received his PharmD from the University of Turin, Italy, where he specialized in chemical and pharmaceutical technology, and his PhD in pharmaceutical sciences from Paris-South University, France. He has 14 years of experience in modeling and simulation of drug effects and clinical trials in industrial and academic settings. Donato has authored 2 books, 2 book chapters and contributed to more than 13 publications in international journals. He is currently PBPK Scientific Expert at Sanofi.

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Letizia Carrara (PhD - Servier)

Letizia Carrara is a Senior Pharmacometrician in the Clinical Pharmacometrics group at Servier, in Paris. She is an Engineer and in 2018 she received a PhD in Bioengineering and Bioinformatics at the University of Pavia (Italy). During the PhD she worked on several projects, both in preclinical and clinical settings, in oncology and infectious diseases, and she spent 6 months as a visiting scientist at the University College of London (UCL). She has 4-year experience as a pharmacometrician, and her main areas of expertise are Physiologically-Based Pharmacokinetic (PBPK) modelling for first time in human (FTIH) predictions, drug-drug interaction (DDI) simulations, IVIVC, dosing in special populations, absorption modelling and food effect predictions in oncology and CNS diseases

Oliver Hatley (PhD - Certara)

Oliver Hatley is a Principal Scientist who has been working at Certara UK Limited's Simcyp Division since 2013. He received his MSc in Drug Discovery Skills at the Kings College London in 2009. He went on to study in vitro to in vivo (IVIVE) extrapolation of Intestinal Metabolism with the University of Manchester (CAPKR) and AstraZeneca, focusing on IVIVE scaling factors, receiving his PhD in 2014. Oliver is part of the translational sciences in DMPK group within the Simcyp Division. He has lead development of the esterase organ and blood IVIVE scaling strategies and the development of special adult populations within the Simcyp Population-based Simulator.

Stephan Schaller (ESQlabs GmbH)

Stephan Schaller is the Founder and Managing Director of ESQlabs GmbH, a mid-size biosimulation solutions and services CRO and holds a PhD in Computational Engineering. He has > 15 years of industry experience with a focus on Model-Based Drug Development (MIDD) and Next-Generation Risk Assessment (NGRA). His scientific career is focused on advancing knowledge- and mechanism-based modeling approaches such as PBK, and QSP/T for decision-making support to R&D teams in the Life Sciences. Stephan is the current chair of www.Open-Systems-Pharmacology.com, an initiative to democratize and develop open-source computational tools for physiologically- and

mechanism-based analysis of disease and kinetics and effect of drug therapies and chemicals. Stephan is the coordinator and PI of a number of German national and European multinational public grant research projects.

Facilitator Biography

Laurence Del Frari has over 25 years of experience in modelling & simulation in

Pharmacokinetics and Pharmacodynamics applied to pharmaceutical research and development across various disease areas, including small and large molecules. She has worked in several pharmaceutical companies. Currently, she is expert in PKPD modelling & simulation at Pierre Fabre Laboratories, where she is contributing to the early and late development and registration of new oncology and dermatology drugs. In this role she is responsible for modelling & simulation strategy in drug development, including population approach, Physiologically based pharmacokinetic modelling as well as well as Quantitative System Pharmacology and contributions to trial protocols, analysis plans, study reports and regulatory submissions. With a Pharmacy diploma from Paris University and a specialization in pharmacokinetics & metabolism and in statistical modeling and simulation, her focus is to promote and apply innovative methods to optimize data knowledge, trial efficiency and support investment decisions in drug development

Virginie Gualano (PharmD, PhinC Development)

Virginie Gualano is co-founder of PhinC Development. She is a Pharmacokinetic, PBPK

expert, and Consultant in Pharmacometrics. She has developed the PBPK practices within the company since 2012 and she manages the PBPK unit. With more than 25 years of experience, she held many positions in pharmaceutical industry as a PK project leader, Head of the Pharmacokinetic unit and Pharmacometrician. She is a Doctor in Pharmacy and she holds two university degrees in Pharmacokinetic and in Biostatistics.

Corentin Mit (PhD, PhinC Development)

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Corentin Mit is a pharmacometrician and PBPK specialist at PhinC Development since late 2022. He works on various PBPK applications, including First-in-Human studies, food effect, and drug-drug interactions (DDIs). He completed his doctoral thesis at a national institute specializing in the industrial environment and risks. In particular, he developed several PBPK models in model species to assess exposure to various chemical substances, such as pesticides and plasticizers. Corentin holds an engineering degree in statistical modeling and a doctorate in environmental sciences.