**State of the Art in Model Informed in Drug and Generics Development**

**SEMINAR: 3rd June 2025, 9.00 am**

**VENUE: TBA**

**Summary**

This seminar is intended for academics, students or scientists working in pharmaceutical industries, regulatory agencies, and contract research organizations.

The first Session of the seminar focuses on Recent Advances in MIDD Approaches.

*First Talk:* This presentation summarizes some of the challenges one faces when extrapolating pharmacokinetics from adults to children, in particular when age-/and disease related absorption processes contribute to interindividual differences in systemic exposure. Here we aim to highlight the gaps in data and implications such gaps have for the choice of model parameterization and identification of maturation processes and other factors that affect pharmacokinetic disposition in children.

*Second Talk:*Middle-out approaches in PBPK modeling combine bottom-up and top-down approaches. Middle out approaches are used to enhance the predictive accuracy and extrapolate the lung pharmacokinetics of antituberculosis drugs from animals to humans.

*Third Talk:*Single objective/reward approaches to guide model search using composite objective functions have been criticized as potentially arbitrary.  Multiple objective searches allow for the determination of non-dominated trade-offs in model performance characteristics that provide the modeler/user with the “best” solutions for a given set of model performance criteria.  This talk will present approaches based on evaluating 2 or more features simultaneously for population PK models.

*Fourth Talk:*Automatic differentiation (AD) is an alternative to the traditional method of finite difference for calculating gradients in nonlinear regression. We apply AD to the conditional step in mixed-effect nonlinear regression. The results suggest improved performance without loss of robustness.

The second Session of the seminar focuses on MIDD approaches based on the Finite Absorption Time (F.A.T.) concept.

*First Talk:* The science behind the Finite Absorption Time (F.A.T.) concept as well as the development/application of the pertinent Physiologically Based Finite Time Pharmacokinetic (PBFTPK) models is described. The models were built on three principles i) drugs are absorbed passively under sink conditions for a finite period ii) time absorption constrains linked with the gastrointestinal transit times of drug in the stomach, the small intestines and the colon were applied and iii) drug absorption follows zero-order kinetics because of the rapid blood flow (20-40 cm/sec) in the portal vein.

*Second Talk:* In this talk, we first uncover, using the F.A.T concept, the true meaning of *C*max and parameters after a 72-year-long journey of misconception. Then, F.A.T.-driven MIDD approaches used in phases I-III of drug development are described. Emphasis will be given to changes in Phase I of drug development based on the estimation of absolute bioavailability using the F.A.T. concept as well as the use of PBFTPK models as structural models in Phases II and III dealing with pharmacokinetics, pharmacodynamics and pharmacometrics.

*Third Talk:* The strategy of generics development changes. The *in vivo* data of the reference product are analyzed using PBFTPK models and correlated with their *in vitro* data. The development of generics relies on the IVIVC of the reference product. Model dependent and model independent approaches using novel metrics are developed for bioequivalence assessment.

*Fourth Talk:* Abacavir, a nucleoside reverse transcriptase inhibitor used in the treatment of HIV-infected children, exhibits complex pharmacokinetics influenced by developmental changes in drug metabolism. Traditional pharmacokinetic models may not fully capture the absorption characteristics in this population*.* PBFTPK models were used tocharacterize the pharmacokinetics of abacavir in infants, toddlers and children using population analysis in PhysPK®. This is the first application of population analysis using PBFTPK models.

*Fifth talk:* The last talk will be a description and demonstration of the recently developed stand-alone piece of software that performs parameters fitting into a variety of models on phamacokinetic data based on the F.A.T. concept. Participants can bring concentration, time data sets of extra vascularly administered drugs for testing.

**PROGRAMME: State of the Art in Model Informed Drug and Generics Development**

|  |  |  |
| --- | --- | --- |
| Time | Speaker | Topic |
| 8:55 | Panos Macheras | Welcome |
| 9:00 | **Session A** | Recent advances in MIDD approaches |
| 9:00 | Oscar dela Pasqua  Clinical Pharmacology & Therapeutics Group, UCL, London, UK  Clinical Pharmacology Modelling & Simulation, GSK, London, UK | Extrapolation in the Data Desert:  Interindividual Variability in Absorption Processes and Characterisation of Systemic Exposure in Children. |
| 9:30 | Aris Dokoumetzidis  Department of Pharmacy, National and Kapodistrian University of Athens, Greece and PharmaInformatics Unit, ATHENA Research Center, Athens, Greece | The use of middle-out PBPK modelling to extrapolate lung pharmacokinetics of antituberculosis drugs from animals to humans |
| 10:00 | Robert Bies  School of Pharmacy and Pharmaceutical Sciences, University at Buffalo, USA | Multi-objective optimization for population PK models |
| 10:30 | Mark Sale  Certara Organization | Model informed drug development: Performance issues in machine learning, automatic differentiation as a possible solution |
| 11:00 | Coffee break |  |
| 11:15 | **Session B** | MIDD approaches based on the Finite Absorption Time (F.A.T.) concept |
| 11:15 | Athanasios Tsekouras  Department of Chemistry, National and Kapodistrian University of Athens. Greece and PharmaInformatics Unit, ATHENA Research Center, Athens, Greece | From the inception of Finite Absorption Time concept to the development of Physiologically Based Finite Time Pharmacokinetic (PBFTPK) models |
| 11:45 | Panos Macheras  Department of Pharmacy, National and Kapodistrian University of Athens. Greece and PharmaInformatics Unit, ATHENA Research Center, Athens, Greece | The Finite Absorption Time (F.A.T.) Concept I: A new Model Informed Drug Development (MIDD) world is emerging in all phases of drug development |
| 12:15 | Panos Macheras  Department of Pharmacy, National and Kapodistrian University of Athens. Greece and PharmaInformatics Unit, ATHENA Research Center, Athens, Greece | The Finite Absorption Time (F.A.T.) Concept ΙI: A paradigm shift in generics development and bioequivalence assessment |
| 12:45 | Sergio Sánchez-Herrero  Department of Computer Science, Multimedia and Telecommunication, Universitat Oberta de Catalunya, Barcelona, Spain; Simulation Department, Empresarios Agrupados Internacional S.A., Madrid, Spain | Population pharmacokinetics Finite Absorption Time (F.A.T.) model of abacavir in infants, toddlers and children with PhysPK® |
| 13:15 | Nikos Alimpertis1 & Athanasios Tsekouras2  Department of Pharmacy1 and Chemistry2, National and Kapodistrian University of Athens. Greece | FTPK Software: Demonstration |
| 14:00 | End |  |

**Registration-Fees**

* Industry, CROs : 300 €
* Academia-Government: 150 €
* Student: 50 € (Students will receive a certificate at the end of the meeting)