CERTARA®

Simcyp

REGISTRATION DEADLINE
10th November 2017

11th to 15th December 2017

Intensive workshops on

Model-informed drug development:

Incorporating population variability into mechanistic prediction of PK and modelling PK-PD



The model-informed approach to various aspects of drug development is rapidly being adopted by the leading pharmaceutical companies.
The Simcyp workshops focus on the optimal use of compound-specific *in vitro* and *in vivo* data together with system specific information related to humans to simulate and understand drug behaviour in various target populations. This integrated approach informs decisions related to Investigational New Drugs and assists with the conduct and optimal design of clinical studies. The ultimate aim is to better understand drug PK/PD properties, reduce the cost and time of drug development, improve the quality of regulatory submissions and eventually implementing precision medicine.

Delegates will learn how to simulate:

- Metabolic drug clearance (CL)
- Metabolic drug-drug interactions (DDIs)
- Gut first-pass metabolism
- Oral drug absorption incorporating food effects and the impact of dosage form
- Effect of transporters and enterohepatic recirculation on kinetics and DDIs
- Drug distribution to different organs
- Population variability in drug concentration-time profiles
- Variation in kinetics in specific populations (paediatrics, ethnic groups, various disease populations)
- Modelling of therapeutic proteins
- Pharmacodynamic effects of different compounds
- Time-course of drug in plasma that fits observed clinical data (achieved by combining fitting techniques with IVIVE, PBPK and drug specific *in vitro* data)



Model-informed drug development:

Incorporating population variability into mechanistic prediction of PK and modelling PK-PD

Who should attend?

Model-informed drug development has been identified by the FDA as a valuable tool to improve efficiency in drug development and tackle high costs and low success rates[1]. Therefore, our workshops are relevant to senior level managers as well as scientists working in the fields of drug metabolism, ADME, clinical pharmacology, pharmacokinetics, PBPK and PK/ PD, both in industry or in academia and research institutes. There is a focus on facilitating communication and interaction between pre-clinical *in vitro* groups and those responsible for the conduct of early clinical studies. The courses provide a solid grounding in model-informed approaches and are not aimed solely at individuals who have hands-on experience.

What are the benefits?

Participants will learn about the application of 'prior knowledge' to improve the selection and design of clinical studies. The workshops are designed to provide the necessary understanding and skills to simulate and predict the pharmacokinetics of drugs in any relevant populations and assess pharmacodynamic effects at an early stage.

How are the workshops run?

The course is comprised of lectures – delivered by leading experts in each field of PK and PD – interspersed with interactive workshops and demos centred on practical examples of model-informed approaches. Delegates work in small groups with an expert tutor. Non-Simcyp users are guided through the course, whereas more experienced users benefit from exploring the science and specific algorithms in more depth through discussions with tutors and peers.

Registration deadline - 10th November 2017

The workshop runs from 8am to 6pm Monday to Thursday and 8am until lunchtime on Friday. Registration includes programme materials, refreshments and lunch.

(Approximate timings above are intended as a guideline only and may be subject to change)

Do I need to be from an organisation which is affiliated to the Simcyp Consortium?

You do not need to be from an institute which is a member of the Simcyp Consortium to benefit from our workshops. Each event attracts a range of participants from industry, academia and regulatory bodies.

How do I register if my organisation is a member of The Simcyp Consortium?

Each year Consortium Members are allocated a number of free workshop places (based on the number and type of licenses held). If you are unsure of the membership status of your organisation, or you wish to check your entitlement to, or book, a free place (member organisations only), please contact Kelly Turton (kelly.turton@certara.com). Once your place has been allocated, please ensure that you have filled in the name of your organisation, site and department and ticked the relevant boxes for free places on the registration form or used your unique code online.

[1]Zhang et al., 'Model-based drug development: The road to quantitative pharmacology.' Journal of Pharmacokinetics & Pharmacodynamics 2006. 33(3):369-93

Paradise Hotel
296, Haeundaehaebyeon-ro
Haeundae-gu
Busan, Korea

To reserve accommodation at the hotel please email a completed Hotel Reservation Form to res@paradisehotel.co.kr or telephone +82 51 749 2111~3



The following topics will be covered in the workshop:

***In vitro – in vivo* extrapolation (IVIVE) for metabolic clearance (CL) and quality issues:**
Attendees will make quantitative predictions of metabolic clearance using data from human liver microsomes and rhCYP systems. There will be discussion of non-specific binding, active uptake, differences between *in vitro* systems and aspects of quality assurance related to IVIVE. Scaling from other systems such as hepatocytes and rhUGT will also be discussed.

Quantitative prediction of gut metabolism:
Incorporation of biological variability in the prediction of gut metabolism and first pass effects and the interplay between permeability and metabolism.

Incorporation of information on population variability:
This module will focus on how drug elimination differs between individuals (e.g. special populations: children, different ethnic groups, those with different CYP genotypes, renal failure, cirrhosis and obesity). Elements of the demographic, physiological, genetic and biochemical factors that need to be considered when predicting drug clearance in these groups are described along with practical examples to demonstrate the impact with different drugs.

Prediction of concentration-time profiles and dose non-linearity:
Discussions will focus on the necessary elements for predicting concentration-time profiles and contrasting different modelling approaches. Dose-linearity issues related to metabolism including saturation of different pathways will be considered.

Prediction of metabolic drug-drug interactions (DDIs) – inactivation, induction, suppression and stabilisation of enzymes:
A step-by-step introduction on how to use *in vitro* information on the metabolic routes of drug elimination and the characteristics of the perpetrator drug to estimate the potential for metabolic DDIs. The impact of inactivation parameters, turnover rate constant and dose-staggering on mechanism-based inhibition (MBI), *in vivo* as well as the effect of different *in vitro* input data on the simulation of CYP induction and calibration of new inducers against *in vivo* reference compounds will be explored. Inter-individual variability and how to identify the most susceptible patients will be discussed.

Study design issues:
The conduct of clinical investigations to explore enzyme induction and inhibition within the framework of regulatory assessment will be discussed. The influence of trial design elements on DDIs, prediction of mechanism-based inactivation, induction and multiple DDIs will be demonstrated using practical examples.

Sensitivity analysis, parameter estimation and model fitting:
Attendees will receive guidance on the assessment of the sensitivity of model parameters and assumptions and gain experience with fitting PBPK models to observed clinical data (bridging bottom-up and top-down approaches).

Metabolite kinetics:
An introduction will be given to the importance of metabolites in determining pharmacological outcomes as well as DDIs. Subsequently, IVIVE issues in the prediction of metabolite kinetics will be explored and practical examples of the impact of metabolite kinetics for DDI considered.

Distribution aspects of physiologically-based pharmacokinetics (PBPK):
Physicochemical characteristics are combined with biochemical and physiological features of organs in algorithms to estimate volume of distribution, tissue blood partitioning, and drug concentration time-profiles in different tissues and organs. Further, perfusion- and permeability-limited models and the required systems and drug parameters for liver, brain and kidney will be discussed.

Pharmacodynamics (PD):
The Simcyp PD module will be used to simulate pharmacological responses to drug compounds using simple and advanced pharmacodynamic models including intrinsic efficacy transduction, indirect response and survival models. The impact of variables such as concurrent medication, disease conditions, ethnicity, CYP-enzyme phenotypes and different formulations on the response to the drug will also be investigated.

Prediction of drug absorption and assessment of food effects and dosage form:
This module considers entry of the drug into the enterocyte, gut wall metabolism and the effects of food, both on the physiology of the GI tract, as well as its impact on the processes of drug solubility, dissolution and metabolism. Population variability and the elements that influence oral drug bioavailability are examined using the Advanced Dissolution, Absorption and Metabolism (ADAM) model. Dermal and pulmonary routes of drug administration will also be considered.

IVIVE of transporter-related information and biliary excretion:
Attendees will investigate the effects of intestinal apical uptake and efflux transporters on drug absorption, gut metabolism and DDIs, as well as the impact of hepatic transporters on metabolism, DDIs and biliary excretion considering potential reabsorption of the drug in the intestine. Transport in the brain and kidney, including competitive inhibition of kidney transporters, will also be covered.

Biologics:
Attendees will become familiar with the Simcyp biologics module and the steps involved in simulating data for therapeutic proteins. The effect of target-mediated drug disposition (TMDD) on the pharmacokinetics of therapeutic proteins will be investigated.

Simcyp Animal:
The Simcyp Animal models will be used to assess the PK properties of compounds and simulate concentration-time profiles in the virtual rat, dog, knock-out mouse and monkey.

"The course, as well as the simulator, compiles up-to-date ADME knowledge. It is tremendously useful for PK scientists in both discovery and clinical fields."

Senior Research Investigator, Princeton workshop

"The most significant learning benefits were the applications [of Simcyp] to clinical pharmacology study design and regulatory submissions."

Shanghai workshop attendee

Previous locations include:

Arosa, Philadelphia, Baltimore, Prague, Tokyo, San Francisco, Washington DC, Leiden, Sheffield, La Jolla, London, Princeton, Indianapolis, Konstanz, Basel, Boston, Shanghai, Cambridge, Frankfurt,



Simcyp Workshops
Busan 11th to 15th December 2017

REGISTRATION FORM

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Please complete all sections of this form and fax to: +44(0) 114 2922333 or post to Simcyp Limited, Blades Enterprise Centre, John Street, Sheffield, S2 4SU, UK

Alternatively you can register online at **www.certara.com/resource-library/workshops/**

Title: Professor / Dr / Mr / Mrs / Miss / Ms Gender: Male / Female

First Name: _____ Surname: _____

Company: _____ City: _____

Position: _____ Site: _____

Invoice Address: _____

_____

_____

Telephone: _____ Email: _____

Purchase Order Number: _____ VAT number: _____

Have you used the Simcyp Simulator before? □ Never used it □ Yes, years ago □ Regular user □ Superuser

Package/Option	Member**/ Academic	Non Member	Consortium Member free place/ Teaching license holder place*
Early Registration - before 9th June 2017	☐ $1500	☐ $2000	☐
Standard Registration - 9th June 2017 - 9th October 2017	☐ $1800	☐ $2400	☐
Late Registration - 10th October 2017 - 10th November 2017	☐ $2160	☐ $2880	☐

OPTIONAL SEMINAR

What It Takes to Make Model-Informed Individual Dosing the Common Practice? Sponsored by Certara, PGRC/Inje University, KoNECT, KSCPT
This Seminar will take place on Friday 15th December 2017 and is FREE to workshop attendees. Please confirm your place by checking this box: ☐

Fees are for the full week-long workshops covering all topics listed overleaf. Maximum benefit is obtained from attending the complete course as the material consolidates and builds upon the learning points of previous topics. If you would like to enquire about attending certain parts only please contact Kelly Turton to discuss the options available (kelly.turton@certara.com).

*Free places are available to Consortium members, with agreed reduced rates available for associates with current academic/not-for profit teaching license agreements. If you are unsure of your institution's eligibility for (or allocation of) free/reduced places, please refer to your Simcyp Agreement or contact kelly.turton@certara.com

**as per Simcyp Consortium agreement

Please note: Registration DOES NOT include accommodation

Guests have the capability to book their own reservation by either of the following two methods: by calling our Reservation Department at 1-800 (862)-7728 and using the Booking ID 21296 or through our website using the following link: https://bookings.ihotelier.com/bookings.jsp?groupID=1556124&hotelID=13522

If using the website, the individual guest will need to click on "the "GROUPS" tab, and when asked for their "ATTENDEE CODE", they must enter their Booking ID, which is 21296. Once they select their dates, all of the group information will be displayed.

Payment methods

Your registration invoice will be emailed to your registration address and should be paid within 30 days or prior to attendance at the event (whichever occurs sooner). Seats are not guaranteed until payment is received.
Payment can be made by cheque, bank transfer or online by credit card using the secure payment pages on our members area. If you wish to pay immediately you can register online at **www.certara.com/resource-library/workshops/**

Payment must be received prior to attendance at the event.

TERMS AND CONDITIONS - Registration for this event constitutes acceptance of these terms & conditions

1. "Events" means workshops /seminars/ sessions, as applicable.
2. Registration is inclusive of programme materials, refreshments and lunch.
3. Payment terms: Following completion and return of the registration form, full payment is required within 1 month from receipt of invoice. All payments must be received prior to the event date, or admission will be refused. Due to limited workshop spaces, we advise early registration to avoid disappointment.
4. Substitution: provided the total fee has been paid, substitutions at no extra charge up to 14 days before the event are allowed. Substitutions between 14 days and the date of the event will be allowed subject to an administration fee of equal to 10% of the total fee.
5. Cancellations by the Client must be received in writing 1 month prior to the start of the event in order to obtain a full credit for any future Simcyp event. Thereafter, the total fee is payable and is non refundable. Non payment or non-attendance does not constitute cancellation.
6. Simcyp reserves the right to cancel any event.
7. © Simcyp Limited 2001-2016. Copyright in all workshop material belongs to Simcyp Limited. This material may not be used, sold, licensed, transferred, copied or reproduced in whole or in part or in any manner of form without the prior written consent of Simcyp Limited. The recipient of the workshop material and any confidential information disclosed at the Simcyp event shall undertake to respect and preserve the confidentiality of such information. In all cases, referring to the source of material is mandatory [to be cited as "Simcyp Limited Workshop"]
8. Client information is kept on Simcyp's database and used by us to assist in providing selected products and services which may be of interest to the Client and which will be communicated by letter, phone, fax, email or other electronic means.
If you do not want us to contact you in this way please tick this box. ☐

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