DMDG past Open and Joint meeting programmes

Joint meeting 2022
- in partnership with the GMP (France) & the SPS (Sweden)
3 - 5 October 2022 in Amsterdam

Monday 3 October 2022

10.00 - 12.00 **Registration opens**

12.00 - 13.00 **Welcome lunch (seated in restaurant)**

13.00 - 13.15 **Chairpersons' Opening Address**

13.15 - 14.45 **Session 1. PKPD challenges of New Drug Modalities**

Chair. Rasmus Jansson Löfmark, AstraZeneca; Ben-Fillippo Krippendorff, Roche

Scope.

New therapeutic drug modalities, such as oligonucleotides, cell therapy, gene therapy, gene editing, and PROTACs are breaking therapeutic barriers and are starting to show substantial clinical impact and benefit to patients. Key to the success of these new modalities are desirable DMPK/PKPD properties. While DMPK and PKPD properties of these drug modalities follow established principles of Pharmacokinetics and Pharmadocynamics, new modalities often require rethinking what are important processes and scientifically justified regulatory packages.

The purpose of this session is to address current advancements in DMPK and PKPD insights within these therapeutic classes. It will focus on the very new modalities, pitfalls, tactical considerations, challenges and recent advancements in this highly expanding field.

Speakers.

1.1 PROTACs PKPD. current challenges and critical data for a successful program
Sofia Guzzetti, AstraZeneca Oncology R&D, DMPK, Cambridge, UK

1.2 Towards Development of a Platform PBPK Model for AAV Mediated Delivery of MAb genes
Dhaval K. Shah, Department of Pharmaceutical Sciences, School of Pharmacy and Pharmaceutical Sciences, The State University of New York at Buffalo, USA

1.3 Potential of model-informed drug development and model-based treatment optimization in cellular therapy
Anna McLaughlin, Pharmetheus

14.45 - 16.15 **Session 2. Advantages and challenges of new or repurposed in vitro ADME(T) assays for new modalities**

Chairs. Yannick Parmentier; Christine Bain; Sibylle Neuhoff; Pawel Baranczewski

Scope.

In vitro models aim to reduce/refine/replace the use of *in vivo* studies (3R) and save time and money in the drug development plan. Many new drug modalities are under development and it is a challenge to establish *in vitro* models that are adapted to their own specific DMPK and physico-chemical properties with maximal reproducibility and predictivity of the DMPK/safety and drug interaction risk. This session will focus on the strategies and *in vitro* approaches specifically developed or repurposed for innovative therapeutic modalities, such as oligonucleotides, antibodies, and PROTACs, for predicting their fate and risk of drug-drug interaction. Their values, advantages, limitations, place in the drug development plan and their potential integration into IVIVE-linked physiological-based pharmacokinetic modelling will be discussed.

Speakers.

2.1 Assessment of complex in vitro systems for evaluation of drug-drug interaction risk associated with peptide analogous
Rune Nørgaard, Novo Nordisk

2.2 Advancement in current in vitro models and analysis methods to test ADME of oligonucleotides
Deepak Kumar Bhatt, AstraZeneca

2.3 PROTAC. handle with care
Prof. Gabriele Cruciani, University of Perugia

16.15 - 16.45 **Coffee, Posters, Trade Exhibition**

17.00 - 18.30 **Session 3. DEBATE**

Chair/Moderator/Referee/Lion Tamer. Simon Taylor, Pharmaron UK

Scope.

A recurring theme and unique feature of the DMDG organisations. The legendary DMDG debate returns for another round. There will be someone proposing for the motion and someone proposing against, and we have the audience.

Let the battle(s) begin…!

- This year's motion is.
  "This house believes that with advances in *in silico* methodologies, lab coats will no longer be needed for the DMPK scientists of the 2040s"

Speakers for the motion.

Suzanne Iverson Hemberg, Toxicology Knowledge Team Sweden AB
and
Jamie Henshall, UCB

Speakers against the motion.

Steve Hood, GSK AB
and
Matt Segall, Optibrium

18.30 - 19.15 **Drinks Reception**

EVENING **Dinner (own arrangements)**

Tuesday 4 October 2022

08.30 - 10.00 *Chairs. Etienne Chatelut, Institut Universitaire du Cancer de Toulouse; Caroline Rynn, Roche; Laurence Del Frari, Pierre Fabre Médicament; Sarah Lobet, University of Tours* **Scope.**

The pharmaceutical industry is clearly moving toward more mechanistic and quantitative PK and PKPD modeling to gain a deeper understanding of translational pharmacology. This session will aim to cover quantitative PKPD modeling of immuno-oncology drugs, spanning different modalities, to demonstrate how PKPD modeling has been used to further elucidate the mechanism of action, predict the clinical response and improve compound survival in the clinic.

Speakers.

4.1 Translational PKPD modeling to predict the pharmacological active dose of a novel, targeted, cancer immunotherapy TLR7 agonist
Neil Parrott, Roche

4.2 Early stage Mechanism-based model to guide biologics engineering in immuno oncology. Pro's & limitations
Cécile Ducelier, Sanofi

4.3 Is target-mediated pharmacokinetics of monoclonal antibodies necessary to consider for optimal dosing?
David Ternant, Tours University

4.4 A framework for prediction of progression free survival based on modelling of sub-endpoints
Celine Sarr, Pharmetheus

10.00 - 10.30 **Coffee, Posters, Trade Exhibition**

10.30 - 12.00 *Chairs. Ashwani Sharma, Nazanin Golbamaki, Cornelis Hop*

Scope.

Early determination (pre-clinical) of Drug Metabolism and Pharmacokinetics (DMPK) properties of compounds can improve decision making in drug discovery and selection of more efficacious compounds with appropriate DMPK properties. Both, in-vitro and in-vivo studies are exploited for pre-clinical screening, however, mentioned pipelines are long, complex, and depend on numerous undetermined factors. Our session "Leveraging Machine Learning for DMPK modeling" focuses on providing the impact of Machine Learning in drug discovery and development and DMPK analysis, yielding accurate predictions and insights. Machine Learning models enhance the accurate prediction of favorable physicochemical characteristics (e.g., solubility and permeability), pharmacokinetics (PK), safety, to prescreen covariates in PK-pharmacodynamic data, and possibly efficacy of drug candidates. During our

session, we will discover different applicability domains and limitations of Machine Learning in DMPK modeling.
Speakers.

5.1 The Application of Machine Learning in the Prediction of Drug-Drug Interactions
Venkatesh Pilla Reddy, AstraZeneca, Cambridge

5.2 Predicting PK from Limited *in Vitro* ADME Data using Deep Learning
Matthew Segall, Optibrium

5.3 Combined Machine learning/AI and in vitro method for prediction of fraction unbound in human plasma. Application in DMPK
Françoise Bree, Insight Biosolutions

12.00 - 13.00 **Lunch ("Grab & go" in Atrium), Posters, Trade Exhibition**

13.00 - 14.30 **Session 6. Student Session**

Scope.

Call for abstracts - students, short oral presentations, posters.
We welcome student abstracts in the field of pharmacology (ADME, PK, PD, DDI). All submitted abstracts will be reviewed by the selection committee and chosen to be part of a short-oral presentation (15 minutes) or poster presentation. A “Best Student oral presentation” and “Best Student poster presentation” awards will be announced during the DMDG/GMP/SPS congress 2022. Winners will be designed according to participants' vote (at 60%) and to selection committee vote (at 40%).
The program is open to all students at the Undergraduate, Masters, and Doctoral levels. Non student advisors or collaborators should be acknowledged appropriately, as coauthors or otherwise. However, students are requested to honour the spirit of the program by submitting only work for which they are primary investigators. Presenters must be present during the congress.
Please contact Carla Troisi, Sarah Lobet, Anis Nouichi and Anna Zerdoug for further details.
Speakers:

6.1 Prediction of target mediated PK profile of Bevacizumab in cancer patients using PBPK modelling
Salih Benamara (Marseille University, France) ***(Poster 1)***

6.2 Translational PK of bevacizumab between human and monkey using PBPK modelling
Blaise Pasquiers (Paris University, France) ***(Poster 2)***

6.3 A semi-mechanistic model to characterize the long-term dynamic of HBV markers during treatment with lamivudine and PEG-IFNα
Selma El Messaoudi (Paris University, France) ***(Poster 3)***

6.4 Challenges and PK/PD modelling approaches to support antibody-drugconjugates clinical development
Clémence Pouzin (Lyon University, France) ***(Poster 4)***

6.5 A mechanistic PK/PD model for the characterization and optimization of PROTACs
Robin Haid (ETH Zurich University, Switzerland) ***(Poster 6)***

6.6 Semi-mechanistic modelling shows the impact of structural modifications on the pharmacokinetics of radiolabeled-dendrimers
Jessica Ou (Aix Marseille University, France) ***(Poster 7)***

6.7 Modifying Methotrexate for Osteosarcoma – utilising a metabolism-based approach to identify novel tumour targeted prodrugs
Hannah Spencer (University of Bradford, UK) ***(Poster 9)***

6.8 Leveraging Machine Learning to Quantify Changes in Cellular Localization and Zonal Distribution of Bile Acid Transporters Associated with Nonalcoholic Fatty Liver Disease in Human Liver Tissue
William A. Murphy (University of North Carolina, USA) ***(poster 12)***

6.9 Dose adjustment in patients with liver cirrhosis - comparison of different models
Agustos Ozbey (Katholieke Universiteit Leuven, Belgium) ***(Poster 13)***

14.30 - 16.00 **Session 7. Free Communications**

Chairs. Graeme Scarfe, Sosei Heptares; Sarah Armstrong, Jazz Pharmaceuticals

Scope.

This is an open session for any hot topics or informative case study that you would like to share with the community but may not fit into the themes of any of the other sessions. We would particularly like to encourage Early Career Scientists to use this session to share your

data and gain some experience at presenting in front of a friendly audience. Any topic submitted that is not chosen for an oral presentation, can be presented in the poster session.

Speakers.

7.1 *Ex vivo* evaluation of a nucleotide prodrug for cancer therapy
Alexandra Serre, University of Bradford

7.2 Rational design of polar glycomimetic modalities. A case story of GB1211, the first orally available galectin inhibitor in clinical studies
Fredrik Zetterberg, Galecto

7.3 *In vitro - in vivo* extrapolation of aldehyde oxidase clearance. a systematic analysis and application of empirical scaling
Nihan Izat, Centre for Applied Pharmacokinetic Research, University of Manchester

7.4 Use of selective substrates and inhibitors for rapid assessment of active uptake in drug discovery
Jamie Henshall, UCB

16.00 - 16.30 **Coffee, Posters, Trade Exhibition**

16.30 - 18.00 ***Chairs. Maxime Le Merdy; Olivier Nicolas; Jérémy Perrier; Sibylle Neuhoff; Kunal Taskar***

Scope.

Physiologically based Pharmacokinetic (PBPK) models are mathematical translational tools aiming to reduce costs and to support strategy of drugs in discovery and development. PBPK is also used to inform, predict, and anticipate drug behaviours in sub-populations for whom clinical data may be inaccessible or challenging to obtain. As those models are based on physiological parameters, they represent the ideal tool to study the disease's consequences and disease progression on the pharmacokinetics of active pharmaceutical ingredients. This session will focus on the strategies to implement the impact of diseases on preclinical and human physiologies in a PBPK model in order to predict drugs' pharmacokinetic and impact of sources of PK variability at all stages of a drug product development.

Speakers.

8.1 PBPK modeling to predict oral drug performance in patients with GI diseases
Nikoletta Fotaki, University of Bath

8.2 Breathing New Life into FTiH Dose Predictions using Inhaled PBPK Modelling
Simon Teague, GSK

8.3 Physiologically based pharmacokinetic to Predict Drug Exposure in Malnourished Children
Erik Sjogren, Pharmetheus

18.00 - 18.45 **Session 9. Candle light Lecture**

Chair. Suzanne Iverson, Toxicology Knowledge Team Sweden AB

History of the Candlelight Lecture.

The Candlelight Lecture is a tradition of the PK-Metabolism Section of the Swedish Pharmaceutical Society. The original Candlelight Lecture wasn't named that at all, instead it was the Keynote Lecture of that symposium in the late 1990s (called the Rosenön Meeting). The esteemed Prof. Magnus Ingelman Sundberg was the Chair of this meeting. There was a treacherous snow storm and, at about the time that the keynote lecture was going to start, the power on the island went out. To continue with the lecture, the conference moved to the cafeteria where candles were lit and flashlights were in hand and the lecture was delivered completely analogue, by Prof. Philippe Beaune. Ever since, there has been a so-called Candlelight Lecture where an important contributor to the field of PK and Drug Metabolism has been invited to present their career highlights supported by candlelight, pens and a whiteboard.

In recent years this lecture has been offered in a larger format at Joint Meetings like this one, and admittedly has been augmented with the help of a little bit of electricity. We are now coming back from a pandemic and have become even more dependent on electronic and digital tools. But for now, we will turn off as much as we can and enjoy an "unplugged" lecture for this year's meeting.

Speaker. Ulf Eriksson, AstraZeneca

19.30 boarding **Conference dinner - river boat cruise (optional)**
20.00 seated

Wednesday 5 October 2022

08.30 - 10.00 **Session 10. Deep dive into the ICH M12 guideline on "Drug Interaction Studies"**

Chair. Anna Nordmark, Clin Pharm Consulting; Kunal Taskar, GSK; Vassilios G. Aslanis, Galecto

Scope.

This session will focus on the new ICH M12 guideline on "Drug Interaction Studies". After describing the latest additions, experts from regulatory bodies and from industry will discuss the impact of the harmonization. Specific aspects may include DDI in patients, special populations and administration routes that are not that common. This session may provide an opportunity, through a panel discussion, to discuss DMPK and Clinical Pharmacology aspects for drug interaction assessments to enable addressing specific questions.

Speakers.

10.1 EMA perspective of ICH M12, Drug Interaction Guidance

Elin Lindhagen, Swedish Medical Products Agency (MPA)

10.2 Industry perspective of ICHM12 Drug Interaction Guidance

Sheila Peters, Boehringer Ingelheim Pharma

10.3 The integrated DDI assessment. leveraging modelling and simulation and totality of evidence approaches in situations where conventional approaches are not acceptable

Eva Gil Berglund and Karen R Yeo, Certara

10.00 - 11.30 **Session 11. Drug-Drug Interactions. Next steps towards the harmonization**

Chair. Olivier Nicolas; Mia Lundblad; Kunal Taskar; Rosie O'Keeffe and Yannick Parmentier

Scope.

The purpose of this session is to address the recent research within the drug-drug interaction (DDI) field, also considering the ICH guideline M12, which is under finalization, with focus on the harmonization of substrates, inhibitors and inducers to be used when performing DDI studies of the main drug metabolizing enzymes and transporters. In addition, the clinical implications and significance of the results obtained in vitro will be addressed. The session will pay attention to the strategies to assess DDI risks, not only with phase I metabolites but also phase II metabolites, which can be more prone to cause interactions than the parent drug. Emphasis will also be on emerging trends such as transporter DDI, ADME biomarkers and the use of different cocktail combinations for the simultaneous evaluation of multiple DDI pathways. The optimisation of the different DDI methods and approaches and the understanding of transporter-mediated disposition is of great significance for later clinical development.

Speakers.

11.1 Role of endogenous biomarkers and extracellular vesicles in understanding OATP1B transporter modulation

Sagnik Chatterjee, Ferring Pharmaceuticals

11.2 Endogenous biomarker-informed approach for clinical risk assessment of transporter-mediated drug-drug interactions

Aleksandra Galetin, University of Manchester

11.3 DDI considerations and predictions in specific populations. Pregnancy, Pediatric and diseased population

Farzaneh Salem, GSK

11.4 Highlights of the in vitro sections of the Draft ICH Drug Interaction Studies M12 Guideline and comparison with current guidance

Brian Ogilvie, Sekisui-XenoTech

11.30 - 12.15 **Lunch ("Grab & go" in Atrium), Posters, Trade Exhibition**

12.15 - 13.30 **Session 12. Biotransformation strategies applied to rapid drug development, ASOs, SiRNAs or modified therapeutic proteins**

Chair. Alexander David James, Novartis; Markus Walles, Novartis

Scope.

For the Biotransformation session at this year's open meeting we would like to focus on two main themes.

1. For ASOs, SiRNAs and modified therapeutic proteins, biotransformation data up to now has not typically been included in regulatory filings due to minimal safety concerns associated with these classes of drugs. However there is increasing evidence that biotransformation studies conducted during the drug discovery and

development pipeline may both streamline the lead candidate selection and optimization process and also provide insight into translation from animal models to human. We are looking for speakers who work in this area that would be willing to share case studies around the biotransformation strategies employed in the development of these 'new modalities'.

2. Recently, and particularly during the recent pandemic, there have been several examples of accelerated drug development to support early registrations. We would be interested in discussing biotransformation strategies that need to be considered to support these fast development programs, ideally with examples. What needs to be done and when? Is MIST assessment required? Is a hADME needed to support the initial registration or can sufficient data be generated by other means?

Speakers.

12.1 ADME approaches for the Pfizer oral COVID-19 protease inhibitor program
Amit S Kalgutkar, Pfizer

12.2 AstraZeneca strategy for biotransformation of oligonucleotides during drug development
Mette Lund Pedersen, Astrazeneca

12.3 Biotransformation strategies for the development of Antibody Drug Conjugates
Christian Lanshoeft, Novartis

13.30 - 14.00 **Closing Remarks**

14.00 **Delegates depart**