Current State and Future Expectations of Translational Modeling Strategies to Support Drug Product Development, Manufacturing Changes and Controls

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Faculty Biographies

Andrew Babiskin, Ph.D., currently holds the position of Team Leader for the locally-acting Physiologically Based Pharmacokinetic modeling team in the Division of Quantitative Methods and Modeling (DQMM), Office of Research and Standards (ORS), Office of Generic Drugs, CDER. His current work focuses on advancing mechanistic-based absorption modeling of local-acting complex products to develop/support novel in vitro and in vivo pharmacokinetic-based methods to establish bioequivalence in lieu of a bioequivalence study with clinical endpoints. Dr. Babiskin received his B.S. degree from the University of Maryland (College Park) in Chemical Engineering and his M.S. and Ph.D. degrees from the California Institute of Technology in Chemical Engineering. He joined the FDA in 2012 as an ORISE postdoctoral fellow in the OGD Science Staff (now ORS) and became an employee within DQMM in 2014.

James Butler is a Senior Investigator /GSK Fellow working in Drug Product Development at GlaxoSmithKline. He received a B.Sc. in Applied Chemistry from Nottingham Trent University in 1988, an M.Sc in Pharmaceutical Technology from King's College London in 1991 and a PhD from the Johann Wolfgang Goethe University, Frankfurt in 2012. From 1988 to 1992 James was at Smith & Nephew Pharmaceuticals (UK), working on ophthalmic drug delivery. In 1993 he joined the formulation department of his current company where he has held various roles, including in early development, in oral biopharmaceutics and in the development of predictive tools. In his current role, James advises project teams at all stages of development on oral drug absorption, biorelevant dissolution and other aspects of biopharmaceutics. He has published papers on early stage oral drug development, including on the Developability Classification System (DCS), on poorly soluble drug formulation and on bio-relevant dissolution. From 2012 to 2018 James has been a joint work package leader for the in-vitro tools work-package of the EU funded collaboration IMI OrBiTo (Oral Biopharmaceutics Tools), which had as its vision to "Transform our ability to predict the in vivo performance of oral drug products across all stages of drug development."

Poonam R. Delvadia, Ph.D., has several years of academic, industry and regulatory experience in formulation development and biopharmaceutics through her education and training at the Food and Drug Administration (FDA, 2013-present); Virginia Commonwealth University (Ph.D. in Pharmaceutical Sciences, 2009-2013); Sun Pharmaceutical Advanced Research Company (Research Assistant in Formulation Development, 2006-2008), and Gujarat University, India (Bachelors in Pharmacy and Masters in Pharmaceutics; 2000-2006). Through her Ph.D. research, she developed a novel biorelevant in vitro system to predict the in vivo performance of oral transmucosal dosage forms. As an ORISE fellow (2013-2014) at the Division of Therapeutic Performance (DTP) in the Office of Research and Standards (ORS) of Office of Generic Drugs (OGD) at FDA, she worked towards development of product specific bioequivalence guidances for generic orally administered drugs. She is currently acting biopharmaceutics lead in the Division of Biopharmaceutics\Office of New Drug products (ONDP)

at OPQ\CDER\FDA where she performs the primary and secondary reviews of the biopharmaceutics aspects of the new and generic drug product submissions and involved in biopharmaceutics related research activities.

Prof. Jennifer Dressman's research interests focus principally on translational biopharmaceutics i.e. predicting the *in vivo* performance of drugs and dosage forms after oral administration. She is best known for pioneering the use of Biorelevant dissolution testing and her contributions to combining dissolution testing with physiologically based pharmacokinetic modelling in order to achieve quantitative predictions of oral drug absorption.

In recognition of her research excellence, she has been made a Fellow of the AAPS, the CRS, and the FIP. In 2008 she was awarded the Distinguished Scientist Award of the FIP and in 2017 was named the International Woman Pharmaceutical Scientist of the Year by the APSTJ. Her research papers have been awarded Paper of the Year on four occasions (Ebert Prize 1986, Phoenix Prize 2003, Best Paper Award EJBP 2010 and Most Informative research Paper Simcyp 2017) and she was named a "Highly Cited Researcher" in both 2016 and 2018. She has been invited as a speaker at leading international conferences, universities and pharmaceutical companies on over 200 occasions and has graduated more than 60 doctoral students.

Arian Emami Riedmaier, Ph.D., is a PBPK Group Lead/ Senior Scientist III in DMPK and Translational Modeling. Arian completed her undergraduate and master's studies in pharmacology at the University of Toronto in 2010 and moved to Germany (University of Tuebingen) through a fellowship program where she received her PhD degree in pharmaceutical sciences. Arian joined the DMPK, Translation Modeling department at Abbvie in 2016 where she provides model-based guidance on oral drug absorption, disposition and drug-drug interactions. She has authored various manuscripts and white papers on best practice in PBPK modeling and simulation and is currently leading an IQ-led collaboration on assessing the predictability of PBPK models for understanding food effect.

Dr. Tycho Heimbach is a Director at Novartis where he has lead a global PBPK modeling group in PK Sciences and serves as PBPK and biopharmaceutics expert. He received his Ph.D. in Pharmaceutics from the University of Michigan. Currently he co-chairs a global team which reviews and makes recommendations and conducts predictions to inform clinical trials, including food -effect studies, within the global PK Sciences function. His responsibilities include addressing regulatory questions in biopharmaceutics and BA/BE across therapeutic areas. Moreover, his duties include development of translational biopharmaceutic formulation and PBPK/PD strategies across all development stages as well as performing pediatric dose selections. He served as the Novartis representative on PBPK WGs for PBPK Modeling and

the PBPK renal and hepatic impairment for the Innovation and Quality in Pharmaceutical Development (IQ) consortium and recently co-authored a workshop summary paper on PBBM (Physiologically Based Biopharmaceutics Modeling). Dr. Heimbach contributed to a priori PBPK modeling for 25+clinical trials and has authored/coauthored 15+ IND's. Dr. Heimbach has been a speaker at 35 national and international conferences. He has authored/coauthored 45 peer-reviewed publications, 3 book chapters and 1 patent.

Dr. Maziar Kakhi obtained his Bachelor's degree in mechanical engineering in 1990 and his Ph.D. in 1994 from Imperial College, University of London (UK). He has over eleven years of industrial experience in the automotive and process/chemical engineering sectors (based in Austria and Germany respectively), in areas related to combustion, complex fluid flow analysis, chemical reaction engineering using population balance methods and software development. Since 2005 he has been working at the FDA as a principal investigator focusing on the application of mathematical modeling techniques to the hydrodynamics in dissolution apparatuses, fluid dynamics of inhalation devices, IVIVC modeling (using numerical, stochastic and physiologically-based approaches), and statistical sampling methods for large sample sizes. He has also worked with the Division of Biopharmaceutics as a primary and secondary reviewer.

Filippos Kesisoglou is a Distinguished Scientist at Merck & Co., Inc., Kenilworth, NJ, Pharmaceutical Sciences organization where he is currently leading the preclinical and translational biopharmaceutics team. His work focuses on the integration of formulation, pharmacokinetic, clinical and CMC regulatory considerations to enable drug product development, focusing on drug product quality for the patient. Applying these principles, he has been a key contributor to multiple new drug applications across several therapeutic areas. He holds a diploma in Pharmacy from Aristotle University of Thessaloniki, Greece and MSc and PhD degrees in Pharmaceutics from University of Michigan. He has authored/co-authored more than 70 manuscripts and more than 80 meeting abstracts and podium presentations in national and international meetings in the fields of biopharmaceutics, PBPK modeling, formulation development and drug delivery. He is active in multiple collaborative efforts across industry, academia and regulatory stakeholders including IQ and PQRI working groups, focusing on the application of PBPK modeling and the development of clinically relevant drug product specifications. In 2017 he was elected a Fellow of the American Association of Pharmaceutical Scientists (AAPS).

Edmund Kostewicz works in the Institute for Pharmaceutical Technology at Goethe University. Edmund received a Bachelor of Science from the University of Adelaide in 1992, Honors Degree from Flinders University in 1993 and his PhD was awarded from the University of South Australia in 1997. Following the completion of his PhD, he held a Postdoctoral position at the

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Institute of Pharmaceutical Technology at the Goethe University in Frankfurt for a period of 3 years. Thereafter, he held a position as Research Scientist within the Department of Biopharmaceutics at AstraZeneca (Mölndal) Sweden prior to taking on the position as Project Coordinator within the Centre for Drug Candidate Optimisation at Monash University in Melbourne. In 2009, Edmund accepted his current position back in the Institute of Pharmaceutical Technology at Goethe University in Frankfurt.

Edmund's research interests lie in the use of different in vitro and in vivo tools for predicting oral drug absorption in humans. Not only has he worked extensively with the use of animal models but also in the use of various in vitro tools to predict oral drug absorption in humans. He has a particular interest in evaluating gastrointestinal supersaturation and precipitation and the use of physiologically based pharmacokinetic modeling to translate the in vitro results to an in vivo setting.

Mirko Koziolek is a postdoctoral researcher at the Center of Drug Absorption and Transport (C_DAT) in Greifswald, Germany. He received his PhD in Pharmaceutical Sciences from the University of Greifswald in 2014. Following his doctorate, he spent 12 months in the group of Prof. Christopher Porter at the Monash Institute of Pharmaceutical Sciences in Melbourne, Australia. In 2016, Mirko returned to the group of Prof. Werner Weitschies and continued his research on the in vitro and in vivo characterization of drug release from oral dosage forms. This work includes the design and optimization of biorelevant in vitro tools such as the GastroDuo as well as the application of different in vivo techniques such as MRI or telemetric capsules to study GI physiology and the in vivo behavior of oral formulations in humans. Mirko is author and co-author of more than 30 peer-reviewed publications and is a regular reviewer for various pharmaceutical journals. In the European COST action on "Understanding Gastrointestinal Absorption Processes (UNGAP)", Mirko is co-lead of the working group "Food-drug interface."

Amitava Mitra is Director of Clinical Development at Sandoz, A Novartis Division. He has previously worked in the Biopharmaceutics group at Merck & Co. Amitava graduated with a PhD in Pharmaceutical Sciences from University of Maryland, Baltimore in 2006. Amitava's main research interests include pharmacokinetics, biopharmaceutics, and PBPK modeling & simulation of oral and alternate drug delivery systems. He has interacted with global regulatory authorities on these topics. Amitava has published more than 42 research and review articles in peer-reviewed journals and has given 28 podium presentations in national & international conferences.

Nikunj Patel is a Principal Scientist in modelling and simulations group at Certara UK Limited's Simcyp Division. He joined the Simcyp team in August 2011 and mainly worked on oral and dermal absorption PBPK Modelling and cardiac safety risk assessment. He led development of

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IVIVC module of Simcyp, first version of SIVA biopharmaceutics platform and mechanistic dermal absorption model as part of the US FDA GADUFA Research grant funding. He works as scientific advisor and consultant in the area of biopharmaceutics for pharmaceutical companies. He pursued his PhD at the Jagiellonian University Medical College, Cracow in the field of Quantitative Systems Toxicology and Safety (QSTS). Before joining Simcyp, he worked for 3 years at a Life science IT consultancy company focusing on PKPD modelling and QSAR model development for various ADMET properties.

Xavier Pepin, Ph.D, Principal Scientist, Pharmaceutical Technology and Development, AstraZeneca UK

Xavier is a pharmacist (University Paris XI). He has a Ph.D. in granulation technology where he studied powder surface energy and liquid bridges during wet high-shear granulation. He has more than 20 years' experience in the pharmaceutical industry and has occupied several positions from preformulation, clinical and commercial formulation development, industrial transfer, regulatory CMC and biopharmaceutics. He's worked in biopharmaceutical tools development for 10 years in transversal collaboration with scientists from CMC, Clin Pharm & MPK departments, using in vitro, in silico, and in vivo tools to support biopharmaceutical evaluation of drugs along the development value chain and post marketing. He was the co-leader of WP4 in silico tools for the OrBiTo IMI project 2012-2018.

He has 25 publications in the field of powder surface energy, granulation technology and biopharmaceutics. His hobbies are building homes and furniture… cycling and travelling.

Paul Seo received his BS in Biochemistry from the University of Maryland at College Park in 1999. Shortly thereafter, he received his Ph.D. in Pharmaceutical Sciences in 2004, from the University of Maryland, Baltimore, focusing in the area of biopharmaceutics and pre-formulation. Paul has worked for the FDA for over 14 years, and has gained experience in the Office of Generic Drugs, Office of Pharmaceutical Science, and Office of New Drug Quality Assessment. He currently oversees the direction and review processes of the Division of Biopharmaceutics in the Office of New Drug Products, as they pertain to NDA and ANDA related Biopharmaceutics issues. Additionally, his professional experience included time at the National Institute of Standards and Technology, Shire Labs, Inc., and the Walter Reed Army Institute of Research.

Satish Sharan, Ph.D., is a reviewer in Quantitative Clinical Pharmacology team within the Division of Quantitative Methods and Modeling, Office of Research and Standards, Office of Generic Drugs. He graduated with Ph.D. in Pharmaceutical Sciences from Temple University, School of Pharmacy with major in Pharmacokinetics under guidance of Dr. Swati Nagar.

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Thereafter Dr. Sharan pursued his post-doctoral training in modeling and simulation under guidance of Dr. Sukyung Woo at University of Oklahoma, College of Pharmacy. Dr. Sharan through his training has acquired translational working experience in clinical pharmacology in addition to acquiring advanced modeling and simulation training using physiologically based pharmacokinetic modeling and pharmacokinetic pharmacodynamic modeling and simulation, which is routinely applied at the Division of Quantitative Methods and Modeling at United States Food and Drug Administration to aid in regulatory policy and decision making.

Sandra Suarez Sharp, PhD., is currently a Master Biopharmaceutics reviewer at the Division of Biopharmaceutics/ Office of New Drug Products/OPQ supporting all therapeutic areas. Some of her responsibilities in this office include the secondary/tertiary review of submissions containing Biopharmaceutics information such as dissolution, biowaivers, IVIVCs, multivariate models for RTRT, physiologically based PK-biopharmaceutics models in support of drug product quality, and mentoring new reviewers. She joined the FDA in 1999 as a Clinical Pharmacology and Biopharmaceutics reviewer in the Office of Clinical Pharmacology. Prior to this, she spent two years at UNC Chapel Hill as a postdoctoral fellow in the area of drug delivery to the lungs. Dr. Suarez Sharp holds a Ph.D. in Pharmaceutical Sciences from University of Florida and a bachelor's degree in Industrial Pharmaceutical Chemistry from Mexico.

Lynne S. Taylor is the Retter Professor of Pharmacy in the Department of Industrial and Physical Pharmacy, Purdue University. Prior to moving to academia, she spent several years working at AstraZeneca in Sweden developing new drugs. Lynne received a Bachelor of Pharmacy degree with First Class Honors from the University of Bath in the UK. Her PhD was undertaken at the University of Bradford, UK, in the area of Pharmaceutical Technology. After her PhD, Lynne was a postdoctoral researcher at the University of Wisconsin-Madison. Research in Lynne's group is directed toward exploring the science underlying the preformulation, formulation and manufacturing of drugs and other bioactive substances, in particular poorly water soluble compounds. She has published more than 280 peer reviewed articles. Lynne has received a number of awards including the Coblentz Society Craver Award in Applied Vibrational Spectroscopy (2014), the Journal of Pharmaceutical and Biomedical Analysis Outstanding Manuscript award (2007), the Ebert prize for the best manuscript in the Journal of Pharmaceutical Sciences (2012) and the Pharmaceutical Research meritorious manuscript award (2012). Lynne is a Fellow of the Royal Society of Chemistry and the American Association of Pharmaceutical Scientists, and is editor-in-chief of the ACS journal, Molecular Pharmaceutics.

Christophe Tistaert, PhD, a Principal Scientist Biopharmaceutics in the Small Molecules Pharmaceutical Development organization of Janssen Research & Development. In this role he

is responsible for the implementation of biopharmaceutical development strategies across the portfolio, predominantly focusing on mechanistic absorption modeling and clinically relevant specifications. Christophe joined Janssen in 2012 as a pharmaceutical scientist. He holds a PhD in Pharmaceutical Sciences from the University of Brussels (Belgium) and a master's degree in Pharmaceutical Sciences from the Catholic University of Leuven.

Eleftheria Tsakalozou joined the FDA in 2015 as an Oak Ridge Institute for Science and Education (ORISE) Fellow. She is currently a Staff Fellow at the Division of Quantitative Methods and Modeling at the Office of Research and Standards. Dr. Tsakalozou obtained her PhD in Pharmaceutical Sciences at the University of Kentucky in 2013 and completed a two-year Fellowship in Clinical Pharmacokinetics and Pharmacodynamics at the University of North Carolina at Chapel Hill. Her research interests include skin absorption physiologically-based pharmacokinetic modeling, interactions between excipients and molecular targets including gut transporters and development of quantitative modeling and simulation tools to support bioequivalence assessments.

Christian Wagner studied Pharmacy at the Goethe University in Frankfurt/Main (Germany) and graduated as a Registered Pharmacist in 2009. From 2009 till 2013, Christian was a PhD student in Jennifer Dressman's lab at Goethe University, where he conducted research on applying Physiologically-Based Pharmacokinetic (PBPK) modeling, combined with biorelevant solubility, dissolution, and precipitation methods, to predict the oral absorption of poorly soluble acidic, basic, and neutral drugs. Upon completion of his PhD, Christian joined FDA's Office of Clinical Pharmacology in Silver Spring MD (USA) as a postdoctoral researcher in 2013. As part of his research, he applied PBPK modeling to predict the impact of intrinsic (e.g., hepatic impairment) and extrinsic (e.g., drug-drug interactions) factors on the pharmacokinetics of antiretroviral drugs. In 2015, Christian joined the preformulation group within Merck KGaA in Darmstadt (Germany), where he heads the biopharmaceutics team. Within this position, Christian and his team lead the biopharmaceutical evaluation of Merck's NCE pipeline in Drug Discovery and Development.

Xinyuan (Susie) Zhang, Ph.D., is a PBPK co-lead in the Division of Pharmacometrics (DPM)/ Office of Clinical Pharmacology (OCP)/ Office of Translational Sciences (OTS) / CDER. She shares responsibility for scientific oversight of PBPK review activities and provides leadership in PBPK-related research in OCP. Dr. Zhang has conducted clinical pharmacology reviews for numerous INDs and NDAs. Prior to joining OCP, Dr. Zhang was a scientific lead for absorption modeling in the Office of Research and Standards (ORS)/ Office of Generic Drugs (OGD) / CDER where she focused on applying PBPK absorption modeling and simulation to address issues in Abbreviated New Drug Application (ANDA) reviews, controlled correspondences,

citizen petitions, and bioequivalence guidance development. She received her Ph.D. from the University of Michigan, Ann Arbor.

Dr. Banu Zolnik is a biopharmaceutics acting team lead for the oncology and hematology product in the Office of New Drug Products in Office of Pharmaceutical Quality at the FDA. Prior to joining the FDA, Dr. Zolnik was a post-doctoral fellow in the Nanotechnology Characterization Laboratory at the SAIC/National Cancer Institute/NIH. Dr. Zolnik received her Ph.D. degree in Pharmaceutical Sciences from the University of Connecticut.