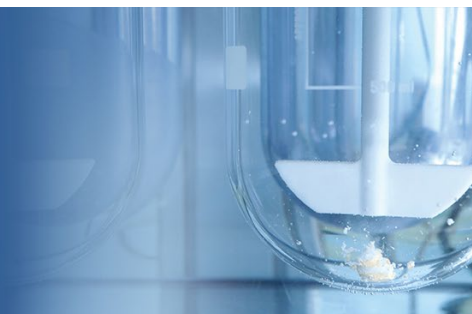


USP Workshops

→ **Advancements in
In-Vitro Performance
Testing of Drug Products**

December 11-12, 2019
USP Meetings Center | Rockville, MD



Speaker Biographies & Abstracts (listed alphabetically)

**Shirlynn Chen, Ph.D.**

Director, External Alternative CMC Development
Boehringer Ingelheim Pharm Inc.
Ridgefield, CT

Shirlynn Chen is a Director in External Alternative CMC Development of Boehringer Ingelheim Pharm. Inc., Ridgefield CT. She received her Ph.D. in Pharmaceutics from the University of Connecticut. Dr. Chen has over 25 years industrial experience in the area of preformulation, formulation development and scale up, and regulatory CMC submission of various oral dosage forms. Her areas of expertise include physical pharmaceutics, preclinical and clinical formulation design and development of complex oral drug delivery systems such as self-emulsifying formulations, solid dispersions, and other approaches for bioavailability enhancement. Dr. Chen has published and filed patents in the field of improving dissolution/solubility and oral bioavailability for poorly soluble compounds. Dr. Chen is currently responsible for drug product development in support of the global project portfolio, by developing new CMC project strategies for more effective NCE development and for advancement of NCE-like alternative medicinal therapeutic product projects.

Presentation***Bio-relevant In vitro GI Model (TinyTIM-1) for Food Effect Prediction***

Wednesday, December 11, 2019, 1:30 – 2:00 p.m.

Standard in vitro methods are limited in their ability to simulate the dynamic aspects of in vivo dissolution of a dosage form during transit through a rapidly changing and complex gastrointestinal (GI) environment, especially when effect of food is involved. In this presentation, an advanced in vitro model, tiny TIM-1 (tTIM-1), was evaluated for its feasibility to predict in vivo bio-performance of solid oral formulations under fast and fed conditions. The in vitro TNO gastrointestinal model (TIM-1) is a computer controlled in vitro GI system that simulates stomach and upper GI tract with physiologically relevant parameters. The tiny-TIM system is a simplified version of TIM-1 eliminating unnecessary complexity as with TIM-1. Two low-solubility compounds (a weak base and a weak acid) in tablet dosage forms at various doses were tested. For the fed state, tablets were given with a standard high fat meal as recommended for clinical studies by the FDA. The amount of the dissolved drug in the intestinal chamber, collected after filtration through a semipermeable membrane per time period, was considered as the fraction available for absorption (bioaccessible amount). The bioaccessibility profiles of the drug were compared with human data. In the first example, clinical data show that both AUC and C_{max} plateaued out with increasing dose in fast condition and positive food effect was observed in fed condition and this food effect is more significant at higher dose. The bioaccessible amounts generated with tTIM at various doses show a strong correlation with in vivo AUC for both fasted and fed conditions. However, the food effect ratios (fed/fasted) predicted by tTIM-1 are less than those in vivo especially at higher dose. This compound is known to be a substrate of Pgp Efflux pump. The higher human food effect ratios suggest that other physiological mechanisms such as food-induced competition or inhibition of Pgp transporters may play a role in addition to solubilization by food. For the tTIM-1 system, sample filtration rate (a surrogate for permeability) could have great impact on measured bioaccessibility. For this compound, a higher sample filtration rate instead of a standard filtration rate of 3 ml/min may further improve food effect prediction accuracy. In the 2nd example, in vitro solubility data show a lower solubility in simulated fed state media than in fasted state media, suggesting a potential negative food effect. The tTIM data show a higher bioaccessible amount and a delayed T_{max} in fed condition which are consistent with human data. In this case solubility data in simulated fasted and fed media do not reflect in vivo observed food effect. One possible explanation for the observed positive food effect (both in vivo and tTIM-1) may be due to the food digestion process where change in lipid/digestion product composition during digestion favors drug solubilization resulting in higher drug concentration in the intestine lumen available for absorption. The tTIM-1 is a useful in vitro tool in predicting in vivo performance of oral formulations during drug product development.

**Martin Coffey, Ph.D.**

Member, USP General Chapters-Physical Analysis 2015 Expert Committee

Research Fellow
Bausch and Lomb
Rochester, NY

Martin Coffey currently leads the ophthalmic products formulation group at Bausch + Lomb in Rochester, NY.

Martin Coffey has worked in the pharmaceutical industry for 20 years in various roles including Analytical Development, Formulation Development, and Product Development Team Lead. His key areas of technical expertise include physical analysis methods, rheology of semisolids and gels, particle size reduction methods for API, manufacturing scale-up, stability evaluation, antioxidant selection, antimicrobial preservation of formulations, surface and colloid chemistry, and physical chemistry. His product development experience includes a wide-range of pharmaceutical products including immediate-release and extended-release oral formulations, topical formulations, ophthalmic formulations, otic formulations, and injectable formulations. Additionally, he has experience on NDA and ANDA products, 510(k) products, OTC drug products, and cosmetic products.

Martin also volunteers his time as a technical expert in pharmaceutical development. He is currently serving as an expert committee member for the USP 2015 – 2020 term on the General Chapters – Physical Analysis committee. He was recognized for his significant contributions to USP by receiving the Thomas S. Foster Award.

Martin Coffey has a Ph.D. degree in Physical Chemistry from the University of Wisconsin--Madison, Madison, WI and a BA in Chemistry from Wabash College in Crawfordsville, IN.

Day Two Moderator

Thursday, December 12, 2019

**Przemyslaw Dorożyński, Ph.D., D.Sc.**

Professor
Pharmaceutical Research Institute
Warsaw, Poland

Przemysław Dorożyński Ph.D, D.Sc. pharmacist, professor of pharmaceutical technology, former scientific director and chief director of Pharmaceutical Research Institute, Warsaw Poland, scientist at Medical University of Warsaw. The author of numerous of works concerning mass transport within polymeric matrix systems during dissolution, application of novel excipients e.g. metal organic frameworks, theranostics and applications of various imaging modalities in formulation development.

Presentation***3D Printing for Fast Prototyping of Pharmaceutical Dissolution Testing Equipment for Nonstandard Applications***

Wednesday, December 11, 2019, 9:30 – 10:00 a.m.

Purpose of the presentation is to discuss the feasibility of 3D printing techniques for development of analytical equipment dedicated for specific dosage forms and for nonstandard applications. As a working example the results of rapid 3D prototyping of dedicated, MRI-compatible dissolution equipment for mucoadhesive buccal tablets will be presented. Rapid prototyping techniques were found to be a fast, inexpensive way to develop a dedicated dissolution testing setup. The development of the 3D printed setups for dissolution studies is a part of the project (NOMAD-L), which is dedicated development of innovative testing methodology for drug products under development.

**Tapash Ghosh, Ph.D.**

Quality Assessment Lead, Biopharmaceutics
U.S. Food & Drug Administration
Silver Spring, MD

Tapash K. Ghosh, Ph. D. is currently employed at the Office of Pharmaceutical Quality (OPQ), at CDER, FDA. Before working at OPQ, he was at the Office of Clinical Pharmacology (OCP) at CDR, FDA. Before joining FDA, he held faculty positions in two academic institutions and also worked briefly in pharmaceutical industries. He is in the expert panel of USP. He authored numerous scientific publications and delivered scientific speeches nationally and internationally on different scientific topics related to drug development. He is also the editor of four scientific books, all published by the CRC press in their pharmaceutical science series.

Presentation***In Vitro Performance Testing for Intra-uterine, Topical and Transdermal Dosage Forms from the Biopharmaceutics Review Perspective***

Thursday, December 12, 2019, 11:00 – 11:30 a.m.

Development of dermal and intra-vaginal delivery systems is one of the most exciting and challenging areas of pharmaceutical research. Tests for these drug products are divided into two categories: (1) those that assess general **product quality** attributes, and (2) those that assess **product performance**, e.g., *in vitro* release of the drug substance from the drug product. Quality tests assess the integrity of the dosage form, and performance tests, such as drug release, assess attributes that relate to *in vivo* drug performance. Taken together, quality and performance tests are intended to ensure the identity, strength, quality, purity, comparability, and performance of these drug products. This presentation will discuss *in vitro* performance testing for intra-uterine, topical and transdermal dosage forms based on FDA's current Biopharmaceutics Review Perspective.

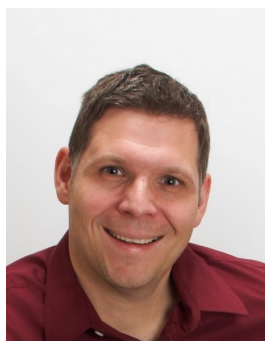
**Paul W S Heng, Ph.D.**

GEA-NUS Pharmaceutical Processing Research Laboratory
Department of Pharmacy, National University of Singapore
Singapore

Dr Paul W S Heng has a basic degree in pharmacy and obtained his PhD from the National University of Singapore in 1985. He has since joined the Department of Pharmacy, National University of Singapore as a faculty member, and teaches pharmaceutical technology for three decades. He served as Head of Department for two terms, 2000-2004 and is the Principal Investigator for GEA-NUS Pharmaceutical Processing Research Laboratory, a research laboratory focused in process and product development related to pharmaceutical technology. Dr Heng has served several terms as Chairman of the Singapore's Quality Control Advisory Committee which saw the acceptance of Singapore as a member of the PIC/S. His research interest is in pharmaceutical technology, especially research related to solid dosage forms, particulates, pellets and tablets. He has expertise with excipients, design of controlled release systems, inhalable systems, encapsulation technologies as well as various product quality testing such as flowability, dissolubility and stability. He has successfully supervised or co-supervised over fifty doctorate program students, several masters students, authored or co-authored over 290 international refereed research journal articles and has also written several book chapters and patents. He is the editor-in-chief of the Asian J Pharm Sci and is in the editorial boards of the Pharm Dev Tech, J Microencapsulation, Drug Dev Ind Pharm, Therapeutic Delivery, AAPS PharmSciTech, J Pharm Sci, Int J Pharm, among others.

Presentation***Dissolution of Inhalers***

Thursday, December 12, 2019, 2:00 – 2:30 p.m.

**Andre Hermans, Ph.D.**

Member, USP New Advancements in Product Performance Testing Expert Panel

Director, Analytical Sciences
Merck & Co., Inc
Rahway, NJ

Andre Hermans is a Director in the Analytical Sciences Division at Merck and Co. in Rahway, NJ. He received his PhD from the University of North Carolina in Chapel Hill in Analytical Chemistry before joining Merck in 2007. During his time at Merck, Andre supported analytical method development and process development in the small molecule solid oral dosage area. In this function, he co-authored several IND and NDA applications mainly for formulations containing amorphous solid dispersions. Additionally, he is co-leading Merck's efforts around in-vivo predictive technologies, dissolution innovations, and clinically relevant specifications. Andre is a member of the IQ dissolution and ICH Q3D workgroups, and a member of the USP expert panel for "New Advancements in Performance Testing". He is author of several publications in the field of dissolution testing and clinical relevance.

Presentation***First-Principles Approaches and Surrogate Testing for Predicting In Vitro Dissolution***

Wednesday, December 11, 2019, 9:00 – 9:30 a.m.

Dissolution modeling based on either first principles or empirical/surrogate measurements can be a very powerful tool during drug development to gain fundamental and mechanistic understanding on how the dosage forms dissolve and which method parameters and product properties influence the dissolution performance. These models can then further be developed and utilized to build control strategies around dissolution performance and possibly enable replacement of dissolution testing for quality control purposes. This presentation outlines possible approaches and explains how to develop empirical and mechanistic dissolution models during various stages of drug development. Several examples ranging from immediate release solid oral dosage forms to extended release tablets and long acting implants are presented.

**Guenther Hochhaus, Ph.D.**

Professor, Pharmaceutics
University of Florida, College of Pharmacy
Gainesville, FL

Dr. Hochhaus received his Ph.D. in 1984 at the Institute of Pharmaceutical Chemistry, Westf. Wilhems University (Münster, Germany). He completed a postdoctoral fellowship at the University of California-San Francisco and subsequently joined the University of Florida's College of Pharmacy as an Assistant Professor in 1987, where he continues to serve today as a Professor of Pharmaceutics.

Dr. Hochhaus' research is interested in evaluating inhalation drugs through in vitro and pharmacokinetic/dynamic approaches, both in animal models, healthy subjects and patients. He evaluated drug, formulation and device factors important for pulmonary targeting and is interested in designing strategies for developing inhalation drugs with high pulmonary selectivity. He currently collaborates with regulatory authorities to improve methodology for drug approval of generic inhalation drugs and is member of the PQRI working group for the development of a biopharmaceutical classification system for inhalation drugs.

Dr. Hochhaus is a Fellow of the American Association of Pharmaceutical Scientists (AAPS) and the American College of Clinical Pharmacology (ACCP). In 1998, he was recipient of the young investigator award of the German Airway and Lung Research Society and received ACCP's Tanabe Young Investigator Award and received in 2019 the Bristol-Myers Squibb Mentorship in Clinical Pharmacology Award. He was awarded the University of Florida Foundation Research Professorship in 2006, 2015 and 2019. He has published more than 220 research papers.

Presentation***Dissolution Methods for Orally Inhaled Drug Products***

Thursday, December 12, 2019, 1:30 – 2:00 p.m.

While dissolution tests represent a central in vitro test for the assessment of oral dosage forms, currently neither USP nor FDA currently has incorporated the assessment of the dissolution behavior of orally inhaled drug products. Observations made while developing and subsequently applying the methodology are shared within this presentation.

**Sandra Klein, Ph.D.**

Professor

University of Greifswald, Department of Pharmacy
Greifswald, Germany

Sandra Klein is a pharmacist by training and got her pharmacist's license and her Ph.D. from the Goethe University of Frankfurt. She was a postdoctoral fellow at Eastman Chemical Company in Kingsport/TN, USA and since 2010 is a Professor of Pharmaceutical Technology at the University of Greifswald, Germany. Her current research is focused on developing bio-predictive in vitro models and oral dosage forms for special patient groups, particularly the pediatric and geriatric population. Other research interests include the design of predictive and accelerated test methods for lozenges, vaginal delivery systems and depot parenterals and she has also a strong interest in establishing formulation strategies for enhancing the bioavailability of poorly soluble drugs. Sandra has 20 years of experience in biorelevant dissolution testing and is (co-) author of various original manuscripts and book chapters on this topic. She is a member of AAPS and DPhG, a board member of APV, a core group member of EuPFI, co-lead of the EuPFI biopharmaceutics workstream and the UNGAP specific populations working group and editor-in-chief of DiePharmazie.

Presentation***Dissolution for Products Applied to the Oral Cavity***

Wednesday, December 11, 2019, 3:00 – 3:30 p.m.

Products applied to the oral cavity are formulations that are placed in the oral cavity without co-administration of fluid. They are for instance used to properly administer drugs in patients that face difficulty in swallowing, to avoid first pass metabolism or degradation in the GI tract or to obtain a local action in the oral cavity or throat. In the recent past a variety of novel dosage forms to be applied in the oral cavity have been introduced. Dissolution testing is an essential tool in quality assurance of these products, but for many of the products official dissolution methods do not yet exist. The presentation will provide an overview of the products that are currently described in international pharmacopoeia as well as of the dissolution methods that are currently official. It will further highlight the requirements for quality control methods and biopredictive dissolution methods and how they relate to in vitro dissolution methods for products applied to the oral cavity that have recently been proposed in the literature.



Johannes Kraemer

Member, USP General Chapters-Dosage Forms Expert Committee

CEO
DISSO GmbH
Homburg, Germany

Johannes is the founder and CEO of DISSO, Germany. He is also the founder of the PHAST Group which consists of PHAST with laboratories in Germany and a site in Switzerland. After the merger with Eurofins he was the responsible person for pharmaceutical science in Europe until April 2019.

He is an active member of

- USP General Chapter Dosage Forms Expert Committee (Chair of Subcommittee GC (1088) In Vitro and In Vivo Evaluation of Dosage Forms
- European Pharmacopeia at EDQM Group 12,
- German Pharmacopeia
- FIP Focus Group Dissolution / In Vitro release
- AAPS In vitro Dissolution Drug Release Group

In addition to lecturing and teaching worldwide on dissolution and IVIVC topics, Johannes has published several scientific articles and book chapters on the same topics and co-edited a book on dissolution testing.

Presentation

Updates on IVIVC

Thursday, December 12, 2019, 3:30 – 4:00 p.m.

The General Chapter (GC) 1088 was first published in Pharmacopeial Forum in 1987. Its second version became official in 2013. Actually, the 3rd version is under revision and will be published for comment in spring 2020. This GC is describing the in vitro characterization of drug substances and drug products as well as their in vivo evaluation.

The link of the in vitro to the in vivo performance of drugs is the in vitro in vivo correlation. It may be defined as a predictive mathematical model describing the relationship between an in vitro property of a dosage form (usually the rate or extent of drug dissolution or release) and a relevant in vivo response (e.g., plasma drug concentration or amount of drug absorbed).

The USP Dosage Forms Expert Committee has taken the responsibility to revise the chapter and has majorly dedicated the scientific work to a subcommittee parallel to the revisions of the related General Chapters 1090 and 1092.

In Vitro and In Vivo Evaluation of Dosage Forms: The New Proposal is based on the version of the monograph being official since 2013. It sharpens the focus on those characterization activities that are directed toward the goal of achieving an in vitro in vivo correlation (IVIVC).

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Major revisions are:

1. The chapter emphasizes on evaluations of oral products.
2. Replace the In Vitro Evaluation section with a new section on In Vitro Characterization, which describes the drug substance and drug product characterization and the process to develop a dissolution test. The technical requirements that are necessary for a dissolution test are given.
3. Revise the In Vivo Evaluation of Dosage Forms to provide a discussion of pharmacokinetic profiling and characterization of the pharmacokinetic properties of immediate-release and modified-release products, as well as a brief discussion of the Biopharmaceutics Classification System (BCS) and its use.
4. Delete the Characterization of Drug Substance section on pharmacodynamic properties in recognition that, although important, such information has been previously gathered and is not necessary for the development of an IVIVC.
5. Revise the Characterization of the Oral Dosage Form section on IVIVC to include a figure giving an example of a linear correlation in addition to the example of a curvilinear correlation currently part of this section. The example procedure for developing an IVIVC also is condensed for clarity.
6. Add a Glossary of terms used in connection with characterization of oral solid dosage forms and development of an IVIVC.

After being published in Pharmacopeial Forum (www.uspnf.com), there will be a period for commenting. The comments will help to compile the final version of the Chapter which will become official at the end of the pharmacopeial process. As the GC 1088 is not aiming to be a textbook USP is offering a course on how to establish a scientifically sound IVIVC.

**Hanlin Li, Ph.D.**

Member, USP New Advancements in Product Performance Testing Expert Panel

Associate Director
Vertex Pharmaceuticals
Boston, MA

Dr. Hanlin Li is an Associate Director in Technical Operations at Vertex Pharmaceuticals, located in Boston, MA. Hanlin has a Ph.D. degree in analytical chemistry from Iowa State University, and is currently leading a group working on late phase development and commercial projects. Hanlin has been involved in Marketing Applications of three products with QbD filing and multiple line extension products. Prior to joining Vertex, Hanlin had worked at Pfizer Global R&D, and together has more than 10 years of pharmaceutical industry experience in analytical development, with a special interest in drug product dissolution and risk-based predictive stability.

Presentation***Dissolution Modeling for Real Time Release Testing (RTRT)***

Wednesday, December 11, 2019, 11:00 – 11:30 a.m.

Continuous manufacturing, QbD and Real Time Release Testing (RTRT) are all innovative approaches in pharmaceutical manufacturing. Together they enable better process understanding and ensure high quality of the product. Out of all the critical quality attributes (CQA) for RTRT, modeling for dissolution may be the most challenging, as tablet dissolution is often influenced by many material attributes and process parameters. In this case study, dissolution modeling of a fixed dose combination (FDC) tablet with two APIs is presented. A comprehensive understanding of the drug product formulation and manufacture process is essential to establish the RTRT model. The lifecycle of RTRT models are also discussed.

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John Mauger, Ph.D.

Member, USP General Chapters-Dosage Forms 2015 Expert Committee

Professor & Associate VP for Health Sciences
University of Utah College of Pharmacy
Salt Lake City, UT

John W. Mauger is currently professor of pharmaceuticals and pharmaceutical chemistry at the University of Utah where he also serves as Associate Vice President for Health Sciences. His educational background includes a B.S. degree in pharmacy (Union University, Albany College of Pharmacy) and M.S. and Ph.D. degrees in pharmaceuticals (University of Rhode Island). John's association with USP includes membership on expert committees and service as a member of the USP Board of Trustees where he also served as chair. His research interests include solubility properties of pharmaceutical active ingredients and the application of physicochemical hydrodynamic principles to standards related to dissolution testing. He is an elected fellow of the American Association for the Advancement of Science.

Day One Moderator

Wednesday, December 11, 2019

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Fernando Muzzio, Ph.D.

Member, USP Quality Standards for Pharmaceutical Continuous Manufacturing Expert Panel

Director, NSF ERC on Structured Organic Particulate Systems
Distinguished Professor, Chemical and Biochemical Engineering
Rutgers University
Piscataway, NJ

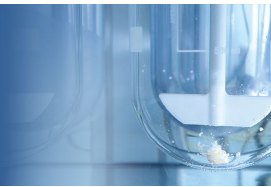
Presentation

A Systematic Approach to Develop Predictive Dissolution Models

Wednesday, December 11, 2019, 10:00 – 10:30 a.m.

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Sarah Nielsen, Ph.D.
Principal Scientist
Janssen Pharmaceuticals
Clinton, NJ

Presentation

Development of Real Time Release Test of Tablet Dissolution

Wednesday, December 11, 2019, 11:30 a.m. – 12:00 p.m.

**Sanjay Patel**

Associate Principal Scientist, Analytical Sciences
Merck & Co., Inc
Rahway, NJ

Sanjaykumar Patel is Assoc. Principal Scientist at Merck & Co., Inc. in Rahway, NJ. He has 18 years of experience in pharmaceuticals industry. His experience includes working on novel drug delivery formulations such as self-emulsifying drug delivery systems, amorphous solid dispersion, controlled release and gastro retentive, and parental formulation. His research interest is focused on developing predictive bio-relevant in-vitro methodologies to understand in-vivo performance of oral and parental formulations. He has co-authored several scientific papers. He is an active member of AAPS and a part of the IVRDT (In Vitro Release and Dissolution Testing) focus group steering committee. He is involved in cross-organization consortium, OrBiTo, in the area focusing on a development and improvement of in-vitro analytical tools.

Presentation***Utilizing Conventional Dissolution Technique to Predictive and Guide Successful Development of Gastro-Retentive Drug Delivery Systems***

Wednesday, December 11, 2019, 3:30 – 4:00 p.m.

Gastroretentive (GR) formulations can be very useful that have the therapeutic efficacy of drugs that have a narrow absorption window, unstable at alkaline pH, soluble in acidic conditions, and active locally in the stomach. The physiological state of the stomach makes it challenging to develop Gastroretentive formulations. There are some products approved using gastrointestinal technologies such as expandable, mucoadhesive, magnetic, ion-exchange resin; and low- and high-density-systems. Given a lack of good preclinical animal models for GR systems makes it imperative to rely on predictive in-vitro analytical tools for optimal pharmacokinetic (PK) performance. Various in-vitro analytical methodologies such as disintegration modified USP I and USP III apparatus were used to investigate drug release mechanisms and swelling/erosion profiles of the GR formulations under fasted/fed state. Formulations robustness was confirmed by performing alcohol-induced dose dumping in FaSSGF/FeSSGF. The performance of GR formulations was evaluated in a flexible clinical study design paradigm for the determination of PK and in vivo gastric retention times via scintigraphy imaging. GR formulations were determined to swell to at least twice their original size within an hour followed by continued swelling to at least 4 times their original size over 9-12 hrs. Based on erosions studies and USP III analysis, drug release from formulations was determined to be via an erosion mediated mechanism. No significant difference in drug release was observed between modified USPI and USP III dissolution ensuring formulation robustness. Furthermore, the formulations were found to be robust to alcohol-induced dose dumping. Preliminary proof-of-concept clinical data demonstrated prolonged gastric retention of up to ~14-16 hours GR formulations with C24 trough concentrations comparable to the IR formulation.

**Katharina Pruessmann**

Ph.D. Student

Center of Drug Absorption and Transport, Institute of Pharmacy

University of Greifswald

Greifswald, Germany

Katharina Pruessmann studied pharmacy from 2006 to 2010 in Tuebingen and obtained her license as a pharmacist in 2011. From 2012 to 2015 she worked as a pharmacist in Hannover. Since 2015, she has been working as a research assistant and Ph.D. student in the Biopharmaceutics and Pharmaceutical Technology department of the University of Greifswald in the working group of PD Dr. Anne Seidlitz. Her main research area is the biorelevant dissolution testing of parenteral dosage forms including drug-eluting stents, subcutaneous implants and cochlear implants.

Presentation***Dissolution of Stents***

Thursday, December 12, 2019, 10:00 – 10:30 a.m.

Drug-eluting stents for coronary application are drug-device combinatory products intended to physically prevent collapse of previously stenosed vessel portions while at the same time locally releasing drugs to prevent re-narrowing caused by hyperproliferation and migration of smooth muscle cells. Upon implantation, the device is in direct contact with the blood vessel wall but also with the flowing blood. However, only drug that reaches the vessel wall tissue will have the desired clinical effect whereas drug released into the blood will most likely be cleared from the site. This presentation addresses the options for dissolution testing of drug-eluting coronary stents and also highlights major challenges associated with this task. Furthermore, experiences of the authors own work with the vessel-simulating flow-through cell, a dissolution test setup especially developed for drug-eluting stents, are shown. This model accounts for the major passive transport mechanisms which are expected to occur upon drug release from stents in vivo (diffusion in the tissue- and convection in the blood-simulating compartment).

**Christos Reppas, Ph.D.**

Professor, Department of Pharmacy
National and Kapodistrian University of Athens
Athens, Greece

Christos Reppas is Professor in Pharmaceutics, Department of Pharmacy, National and Kapodistrian University of Athens (UoA), Greece. He received his Pharmacy Degree from UoA in 1982 and his Ph.D in 1986 from the same University. From 1988 to 1989 he completed a postdoctoral fellowship in Pharmaceutics at the University of Michigan (USA) and then he joined UoA in 1989 as a Lecturer. He has held research positions with the University of London (UK), the University of Michigan (USA), Glaxo R&D (UK) and the University of Frankfurt (Germany). Research interests focus to the effects of gastrointestinal physiology on intraluminal performance of xenobiotics and the development of *in vitro* tests that are predictive of the intraluminal dosage form and drug performance. He has supervised 10 completed PhD Theses and is currently supervising 4. He is coauthor of more than 125 peer reviewed papers in international journals, two books and one patent. He is member of the editorial board of AAPS Journal, Pharmaceutics, Journal of Pharmacy and Pharmacology, Biopharmaceutics and Drug Disposition and Journal of Drug Delivery Science and Technology.

Presentation***The BioGIT System for Assessing the Impact of Dose and Formulation on Early Exposure After Oral Administration***

Wednesday, December 11, 2019, 2:00 – 2:30 p.m.

The BioGIT system and its usefulness will be presented.

BioGIT (Biorelevant Gastro-Intestinal Transfer) system, is an open *in vitro* set-up for estimating apparent drug concentrations and % solid fraction in upper small intestine, after co-administration of a solution/suspension/disintegrating/dispersing dosage form with a glass of water to fasted adults. In case of solution formulation, the % precipitated in upper small intestine is estimated. Using part of the sample collected for measuring apparent drug concentration, apparent equilibrium solubility can further be measured and, therefore, apparent supersaturation in upper small intestine can also be estimated.

BioGIT comprises commercially available equipment and has been shown to be useful in reproducing concentrations measured in the upper SI after administration of solutions, immediate release products, and/or disintegrating enabling formulations. With BioGIT, evaluation of concentrations in the upper small intestine during the first hour after drug administration is possible without the need of *in silico* modeling, e.g. information on the impact of dissolution and GI transfer on formulation performance on a relative basis can be collected or selection of the comparatively more robust formulation can be greatly facilitated. BioGIT data are also useful in the regulatory setting for the evaluation of the impact of dose and formulation on early exposure and for informing physiologically based pharmacokinetic modeling approaches.

**Changquan (Calvin) Sun, Ph.D.**

Vice Chair, USP General Chapters-Physical Analysis 2015 Expert Committee

Professor and Director of Graduate Studies
Associate Department Head, Department of Pharmaceutics
University of Minnesota
Minneapolis, MN

Dr. Sun is a Professor of Pharmaceutics and Director of Graduate Studies at the Department of Pharmaceutics, University of Minnesota. Dr. Sun's research focuses on formulation development of tablet products through appropriately applying materials science and engineering principles. Recent research efforts include 1) crystal structure - mechanical property relationship, 2) crystal and particle engineering for optimizing powder flowability, tabletability, and dissolution. Dr. Sun is an expert in the areas of solid-state science, tablet formulation design, and powder technology. As of December 3, 2019, he has published 166 peer-reviewed papers (H-index = 41) in these areas. He is a member of Expert Committee in Physical Analysis, United States Pharmacopeia. Dr. Sun is an AAPS Fellow and a Fellow of Royal Society of Chemistry.

Presentation***Assessing Dissolution of Oral Tablets Using an Artificial Stomach Duodenum Apparatus***

Thursday, December 12, 2019, 3:00 – 3:30 p.m.

The development of a quality pharmaceutical tablet product of BCS II drugs requires the understanding of dissolution in human gastrointestinal tract. An artificial stomach and duodenum (ASD) apparatus is capable of mimicking GI physiology relevant to drug dissolution, such as pH change, liquid and particle transport, excretion of gastric and intestinal fluids. By accounting for possible complex phenomena induced by those changes, an ASD can be an extremely useful tool to guide formulation development and optimization of tablets with robust *in vivo* dissolution and bioavailability. This talk demonstrates some of the potential benefits of ASD apparatus with recent examples.

**Kailas Thakker, Ph.D.**

Chair, USP Performance Test for Semisolid Dosage Forms Expert Panel

Co-Founder Emeritus
Tergus Pharma, LLC
Durham, NC

Kailas Thakker graduated from Institute of Chemical Technology in Mumbai with a degree in Pharmacy and then went on to earn Masters in Pharmaceutical Sciences from Columbia University in New York and Doctor of Philosophy in Pharmaceutical Sciences from University of Kansas.

She worked at United States Pharmacopeia for 12 years and then went on to head Analytical Department at small, virtual, venture backed biotech company in RTP Area.

In 1994, She founded Analytical Solutions with a vision to provide high quality analytical services to Pharmaceutical Industry. Working with regulatory, compendial and industry leaders, she worked towards developing and improving In Vitro Release Test for topical dosage forms. In 2012, Analytical Solutions was rebranded to Tergus Pharma with a vision to expand the service base by partnering with Dr. Vijendra Nalamothu. Today Tergus Pharma is a world known service provider for topical product, development. After retiring from active duty at Tergus Pharma in 2018, Kailas still continues to advise and assist in developing In Vitro Sciences at Tergus Pharma as Confounder Emeritus.

Presentation***Use of Vertical Diffusion Cells in Dissolution Testing of Suppositories***

Thursday, December 12, 2019, 9:30 – 10:00 a.m.

Dissolution of drugs from suppositories is a complex process involving softening and/or melting of suppository followed by release of the drug form melted mass and into the body cavity. While many approaches are taken to determine the release of drugs form suppositories, no standard method(s) exist. A unique approach using Vertical diffusion cells for a proprietary suppository formulation is discussed.

**Matthias Wacker, Ph.D.**

Member, USP New Advancements in Product Performance Testing Expert Panel

Associate Professor, Department of Pharmacy, Faculty of Science
National University of Singapore
Singapore

Matthias G. Wacker is Associate Professor in the Department of Pharmacy of the National University of Singapore (NUS). Initially, he studied Pharmacy at Goethe University in Frankfurt (Germany) where he obtained his doctoral degree in pharmaceutical technology. As a post-doc and group leader he has joined Jennifer Dressman and Jörg Kreuter in the Institute of Pharmaceutical Technology, Goethe University. There he accomplished his habilitation exploring the 'Rational Formulation Design of Nanocarrier Devices'. Prior to joining NUS, he was heading the Department of Pharmaceutical Technology and Nanosciences of the Fraunhofer-Institute for Molecular Biology and Applied Ecology in Frankfurt. Since 2012, he is a scientific advisor to the editors of the *Journal of Pharmaceutical Sciences*. In 2019, he joined the editorial boards of the *European Journal of Pharmaceutics and Biopharmaceutics* and the *Journal of Pharmacy and Pharmacology* of the Royal Pharmaceutical Society.

Further, has was editing selected issues for the *Beilstein Journal of Nanotechnology* and *Frontiers in Chemistry*. In recognition of his research excellence, he was honored with the Eudragit Best Paper Award in 2014 and the Phoenix Pharmaceutics Science Award in 2017. Recently he was appointed as a new member of the expert panel on New Advancements in In Vitro Performance Testing of the United States Pharmacopoeia. He has published and lectured extensively and organized symposia on various aspects of nanotechnology.

Presentation***Dissolution of Dosage Forms Containing Nanomaterials***

Thursday, December 12, 2019, 9:00 – 9:30 a.m.

After decades of research, an emerging number of biomedical products uses nanotechnology to push the boundaries of drug therapy and to improve the life quality of patients suffering from life-threatening diseases. Unfortunately, manufacturing such therapeutics and monitoring their quality and performance still challenges the current process and analytical technology.

Release testing in combination with *in silico* modelling is a powerful tool in pharmaceutical formulation development. Where do we stand on applying those methods to nanomedicines and what challenges are still out there? The talk will address recent advances in the biorelevant release testing of these versatile dosage forms. Also strategies for establishing an *in vitro-in vivo* correlation not only for peroral formulations but also for injectable nanocarrier systems will be presented.



Daniel Willet, Ph.D.
Division of Pharmaceutical Analysis
U.S. Food & Drug Administration
St. Louis, MO

Dr. Daniel Willett is a chemist at the FDA, Division of Pharmaceutical Analysis in St. Louis, MO. He attended Murray State University where he received a B.S. in chemistry. He received his Ph.D. in analytical chemistry from Clemson University, where he performed research on spectroscopy coupled with nanoparticle synthesis and applications. While at the FDA, he has worked on developing spectroscopic and imaging based approaches in conjunction with multivariate data analysis techniques for physicochemical analysis of complex pharmaceutical products on both the nano and macro scales.

Presentation

In Vitro Characterizations of Topical and Transdermal Drug Products from the Product Quality Assessment Perspective

Thursday, December 12, 2019, 11:30 a.m. – 12:00 p.m.

The special anatomy and physiology of ocular, dermal, and nasal tissues and the complexity of the formulations specific to these areas, has made the clinical end-point evaluations challenging. *In vitro* methodologies such as rheological analysis and *in vitro* drug release/permeation tests were recommended by FDA as alternatives to *in vivo* studies for bioequivalence evaluation of generic and reference listed drug products. Recommendations in the FDA guidance were based on the scientific findings after years of research efforts in method developments to best evaluate product qualities. Moreover, the *in vitro* methods and the guidance are constantly evolving with the advancements in modern technology. For example, advances in spectral imaging has provided a powerful tool for *in vitro* physicochemical characterization for topical and transdermal drug systems (TDS). These tools are particularly powerful for analysis of systems that are heterogeneous in nature (i.e. crystals or different phases and excipients in a topical cream) or that can become heterogeneous post-manufacturing (i.e. crystallization in TDS). This presentation will provide multiple case studies that review the application of advanced *in vitro* methodologies as regulatory research tools to characterize TDS.

Disclaimer

This presentation reflects the views of the authors and should not be construed to represent FDA's views or policies.

**Yang Yang, Ph.D.**

Division of Product Quality Research
U.S. Food & Drug Administration
Silver Spring, MD

Dr. Yang Yang serves as a Principal Investigator and a Chemistry, Manufacturing, and Controls (CMC) reviewer for complex drug products in the FDA's Center for Drug Evaluation and Research. She received her MS in Molecular Pharmacology from Peking University, Beijing and went on to her PhD in Biopharmaceutical Sciences from University of Illinois at Chicago (UIC). She worked at FDA for 6 years. As a reviewer, she is responsible for CMC reviews of numerous topical and transdermal drug products, abuse-deterrent formulations, powder for suspensions and oral solutions. She is also involved in FDA guidance development and providing professional training to FDA reviewers and fellows. She serves as a reviewer for various journals and proceedings for national conferences pertaining to pharmaceuticals and chemistry.

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