Better, Safer, and Cheaper Medicine: A 21st Century Mandate

4 November, 2017

In celebration of 25th Anniversary of the

School of Pharmacy
The Chinese University of Hong Kong

Platinum Sponsor: AMGEN®

Gold Sponsor: Roche

Silver Sponsors: 澳美製藥 香港 Bright Future · Jacobson Pharma Corporation · NOVARTIS · PuraPharm Chinese Medicine Modernized

香港中文大學
The Chinese University of Hong Kong

CU Medicine Hong Kong
香港中文大學醫學院
Faculty of Medicine
The Chinese University of Hong Kong

35th Anniversary 三十五週年

Table of Contents

Foreword

Vincent H.L. Lee
Chair, Organizing Committee
School of Pharmacy
Faculty of Medicine
The Chinese University of Hong Kong

The life sciences revolution is poised to transform healthcare in a radical way. Clinicians now have a better understanding of the complexity of disease to treat patients with precision medicine as a paradigm. Pharmaceutical scientists will gain access to an expanding repertoire of technologies that promise to improve the efficiency of drug discovery and development. Diseases that were once terminal, such as hepatitis C and certain cancers, can now be cured with newly developed and approved medicine. Pharmaceutical and clinical scientists are making steady process to chip away the list of 7,000 rare diseases. It was exciting to note that orphan drugs for rare diseases constituted more than half of the new drugs approved by the FDA of the United States in the past three years … but at a price not even the affluent can afford on a regular basis.

As a measure to contain healthcare costs, biosimilars have emerged as a competitive alternative to the more expensive biologic reference products. Big Pharma is surprisingly as engaged in the biosimilar business as generic drug manufacturers. In part because of the high cost of new medicine, there is now a demand for diagnostics to identify likely responders to precision medicine. Moreover, sophisticated biosensors and complementary digital innovations would enable the remote monitoring – in real time -- of progress in drug therapy of these patients and of exposing behavior aspects that may pose a setback to the prescribed drug therapy, due perhaps to drug-herb interactions. Inevitably, the realms of data from such measurements, collectively named Big Data, and the companion smart inventions of artificial intelligence, machine learning, deep learning, and automation so enabled, will make our dream of "better, safer, and cheaper medicine" come true.

The theme of this one-day forum, **"Better, Safer, and Cheaper Medicine: A 21st Century Mandate"**, is timely. It is a thought provoking topic of immense importance to all of us as consumers, health care providers, scientists, or professionals in the pharmaceutical industry. Coincidentally, the underpinning science upon which this laudable goal is anchored is the subject of the 2017 Nobel Prize in Chemistry, in Economics, and to some extent, in Physiology or Medicine. By highlighting advances in science and technology as well as demographic changes within the confines of one day, the Organizing Committee decided that only those changes on the near term should be covered.

I am optimistic that this forum will set the stage for a continuing dialog and debates that will catalyze necessary disruptive changes in the business model of drug development and regulation. These changes have far-reaching ramifications on not only how pharmacists and pharmaceutical sciences should be educated and trained, but also on redefining the role of healthcare providers, such as pharmacists, in rendering collaborative, team care.

I wish to acknowledge the Organizing Committee for its indispensable role in putting a world class program together. The committee members are Connie Kong of Amgen, Andy Barnett of Roche, and Joan Zuo of CUHK. I would like to thank the sponsors for their generous support that enables us to invite world class scientists and thought leaders from all over the world to participate in this important dialog. The sponsors are:

Platinum	:	Amgen
Gold	:	Roche
Silver	:	Bright Future, Jacobson Pharma, Novartis, PuraPharm
Others	:	Fortune, HK Science and Technology Parks, Pfizer

I hope you will enjoy the forum and be inspired.

Organizing Committee

Prof. Vincent H.L. Lee (Chair)
Mr. Andy Barnett
Ms. Connie Kong
Prof. Joan Zuo

Sponsors

Platinum Sponsor:
Amgen Asia Holding Limited

Gold Sponsor:
Roche Hong Kong Limited

Silver Sponsors:
Brightfuture Pharmaceutical Laboratories Limited
Jacobson Medical (Hong Kong) Limited
Novartis Pharmaceuticals (HK) Limited
PuraPharm Corporation Limited

Other Sponsors:
Fortune Pharmacal Company Limited
Hong Kong Science and Technology Parks Corporation
Pfizer Corporation Hong Kong Limited

Better, Safer, and Cheaper Medicine: A 21st Century Mandate

Date: 4 November, 2017 (Saturday)
Time: 9:00am – 5:30pm
Venue: S.H. Ho College, The Chinese University of Hong Kong
Objective: The objective of the forum is to highlight those scientific advances destined to disrupt the entire supply chain of pharmaceuticals – from discovery to regulation and use. The drivers for change and notable advances in clinical trials, drug discovery, delivery, manufacturing, and regulation will be discussed in the context of the theme of this forum.

Rundown:

Times	Topics	Speaker	Affiliation
8:30am – 9:00am	Registration		
9:00am – 9:05am	Welcome Address	Joan Zuo	CUHK
9:05am – 9:10am	Introduction of the Forum	Vincent Lee	CUHK
	Drivers for Change (Chair: Prof. Joan Zuo)		
9:10am – 9:50am	1. The Role of Genomics and Informatics in Improving the Efficiency of Drug Development	James Creeden	Roche
9:50am – 10:30am	2. The Value of Pharmaceuticals in the Twenty-first Century	Stuart O. Schweitzer	UCLA
	Drug Delivery and Formulation (Chair: Prof. Thomas Lee)		
10:30am – 11:00am	3. Bringing Out the Old but Powerful Ammunition to Tackle Respiratory Infections Caused by Superbugs	Hak-kim Chan	The University of Sydney
11:00am – 11:30am	4. Inhaled Nucleic Acid Therapeutics and Vaccines	Jenny Lam	HKU
11:30am – 12:00nn	5. Polymeric Nanocapsules for Loading and Delivery of Naturally Occurring Agents for Tumor Therapy *in vitro* and *in vivo*	Khuloud T. Al-Jamal	King's College London
12:00nn – 1:30pm	Lunch (The Dining Hall, Morningside College) *The lunch is included in the registration.*		

Times	Topics	Speaker	Affiliation
	Drug Manufacturing (Chair: Dr. Spence Leung)		
1:30pm – 2:00pm	6. Continuous Manufacturing – A Strategy to Make High Pharmaceutical Quality Affordable	Ajaz S. Hussain	Insight, Advice & Solutions, LLC & NIPTE
2:00pm – 2:30pm	7. Next-Generation Biomanufacturing	Arthur C. Hewig	Amgen Inc.
	Drug Regulation (Chair: Dr. Celine Cheng)		
2:30pm – 3:00pm	8. Interchangeability, Who Decides?: Stakeholders, Regional Perspectives and Principles	Thomas Felix	Amgen Inc.
3:00pm – 3:30pm	9. Regulation of Drugs, Devices, and Gene and Advanced Cell Therapy in Japan	Mitsuru Hashida	Kyoto University
3:30pm – 3:45pm	Break		
	Life Cycle Management (Chair: Prof. Vincent H.L. Lee)		
3:45pm – 4:15pm	10. Data Mining and Visualization Techniques for ADME Screening in Early Drug Discovery	Fumiyoshi Yamashita	Kyoto University
4:15pm – 4:45pm	11. Herb-drug Interactions: Impact in Therapeutic Outcome of Integrative Medicine	Joan Zuo	CUHK
4:45pm – 5:15pm	12. Translation of Orphan Disease Trial Design into General Drug Development	E. Dennis Bashaw	US FDA
5:15pm – 5:30pm	Closing Remarks	Vincent H.L. Lee	CUHK

1. The Role of Genomics and Informatics in Improving the Efficiency of Drug Development

James Creeden
Medical Director
Roche Foundation Medicine Inc. – Asia Pacific

BIOSKETCH

Dr. James Creeden is Medical Director for Roche Foundation Medicine and leads Personalized Healthcare strategy for Roche in the Asia-Pacific Region. Previously, he was Medical Director for Roche China, responsible for medical strategy and post-registration studies for the Roche and Genentech portfolio in China, and Chief Medical Officer of Roche Professional Diagnostics. Dr. Creeden holds a PhD in molecular toxicology from Rutgers University and an MD from Robert Wood Johnson Medical School.

ABSTRACT

Cancer therapy has evolved from toxic, one-size-fits-all approaches to today's "precision therapies", and we are learning how to harness the immune system to fight cancer. But not all patients are able to access these potentially life-prolonging medicines - and not only because of cost. Advances in cancer genomics enable us to identify mutations in hundreds of genes from small biopsy samples, and simultaneously transform large patient populations into groups of rare diseases, with the attendant challenges to clinical trial design. The ability to collect and analyze immense databases unlocks our ability to perform real-time evidence collection and make rational policy decisions based on real-world evidence. We will discuss the convergence of several major trends across regulatory decision-making, drug development, cancer genomics and "big data", and the implications for healthcare systems that aim to become world leaders. The most expensive medicine is the one that doesn't work, so as a scientific and policy making community we should be working together to bring the right medicine to the right patient at the right time. I will conclude by highlighting the significant opportunities for Hong Kong to be a global leader in the future of biopharma.

2. The Value of Pharmaceuticals in the Twenty-first Century

Stuart O. Schweitzer
Professor of Health Economics
Department of Health Policy and Management
UCLA Fielding School of Public Health

BIOSKETCH

Stuart O. Schweitzer is Professor of Health Economics in the Department of Health Policy and Management of the UCLA Fielding School of Public Health, Los Angeles. He teaches courses in health economics, health system organization and financing, and pharmaceutical policy. His books include Pharmaceutical Economics and Policy (Oxford University Press), Health Policy and High-Tech Industrial Development (Edward Elgar), Industrial Policy in the United States: Breaking the Taboo (Edward Elgar), and Pharmaceutical Economics (Edward Elgar).

Professor Schweitzer earned his Ph.D. in economics from the University of California, Berkeley. He has taught at Wayne State University and Georgetown University, as well as having been on the research staff of The Urban Institute and the National Institutes of Health. He served as Senior Staff on President Carter's Commission for a National Agenda for the Eighties, where he was responsible for developing national health insurance proposals. In addition, he has held visiting appointments at Oxford University, CREDES (Paris), ESSEC (Paris), and Fudan University (Shanghai). He currently holds a Visiting Professor position at the University of Ferrara, in Italy. His research interests are in the areas of health policy, especially as they pertain to pharmaceuticals, genetics, industrial policy, and the financing of health care. He co-directs the UCLA Research Program in Pharmaceutical Economics and Policy.

ABSTRACT

Medical science is producing startling advances in formerly intractable conditions, including Hepatitis C, Cardiac disease, and many cancers. The age of medical miracles has arrived. Often, treatments extend life and improve quality even if they do not cure a disease or condition. But the cost of health care appears to exceed overall national inflation, so that national share of health expenditures rises – signaling concern. And the cost of pharmaceuticals appears to be rising especially quickly, leading to calls for price controls, which threaten the health of the drug industry, overall national economic performance, and a population's heath status. What can be done about this apparent inconsistency between pharmaceutical progress and our ability to make drugs affordable? This paper will present several ideas.

The first concern is that pharmaceuticals have historically risen in price at a slower rate than other medical and hospital procedures, and pharmaceuticals comprise a far smaller share of national health expenditures than physician and hospital care. We must look elsewhere for the source of rising health costs. We also observe frequently that drug prices are actually too low to maintain R&D and high quality production.

Rising health care costs must reflect both prices and effectiveness. Measuring treatment efficacy is not easy, but is crucial to understand what new treatments do, and what they are worth paying for. Few health systems try to learn what treatments contribute to patient longevity and quality of life, but without this information, health system are unable to set prices that reflect value to patients. The UK has promoted value-based pricing of both drugs and other medical treatments more than other countries, and other countries must study this experience to learn from its successes and failures. Especially admirable was the British attempt to pay for services based on improved length and quality of life, regardless of the nature of condition. This creates a remarkable goal of "fairness" so that patients would receive treatment that worked, regardless of the reason for illness – disease or accident, coronary disease or cancer, or pediatric or geriatric setting.

Only when prices can be set according to value of treatment, and health systems can say that they will not pay for new treatment in the cases in which treatment prices do not reflect outcomes, can systems rationalize expenditures fairly and patients can be treated according to likely improvement in outcomes, and not sociological or political pressure.

3. Bringing Out the Old but Powerful Ammunition to Tackle Respiratory Infections Caused by Superbugs

Hak-Kim Chan
Professor of Pharmaceutics
Faculty of Pharmacy
The University of Sydney

BIOSKETCH

Hak-Kim Chan, Professor in Pharmaceutics, is leading the Advanced Drug Delivery Group at the Faculty of Pharmacy, University of Sydney. He was involved with the product development of Genentech's Pulmozyme (inhaled rhDNase for cystic fibrosis), and Pharmaxis' Aridol and Bronchitol (inhaled mannitol for bronchoprovocation and mucus clearance). His research in pulmonary drug delivery has led to >400 scientific publications (with >10,000 citations) and seven patents. He is an executive editor of *Advanced Drug Delivery Reviews*, a Fellow of the American Association of Pharmaceutical Scientists, and a Fellow of the Royal Australian Chemical Institute. He served as Vice President of the Asian Federation for Pharmaceutical Sciences.

ABSTRACT

Respiratory infections caused by multidrug-resistant (MDR) Gram-negative bacteria ('superbugs') is a major health problem worldwide. Colistin, an old drug effective against these 'superbugs' but with potential systemic side effects, has emerged as the only treatment option in life-threatening infections. Intravenous administration of colistin is known to cause serious side effects in most patients, including renal toxicity. Furthermore, the effectiveness of intravenous administration of colistin against lung infections is questionable, probably due to the sub-therapeutic drug concentrations achieved in the infected respiratory tract. Meanwhile, resistance to colistin in 'superbugs' has reached an alarming level.

Our research used aerosol formulation technology to reposition colistin for respiratory delivery to enhance the treatment outcome. This drug repurposing approach will shorten the drug development time normally required for a new antibiotic. Moreover, targeting antimicrobial therapy directly at the infection site may enhance clinical efficacy while minimizing systemic toxicity.

Besides antibiotics, bacteriophages ('bacteria-eaters') have been documented to be efficacious against MDR bacteria with minimal side effects. We have successfully produced powder aerosols suitable for respiratory delivery of colistin and phages. These powder formulations are stable, highly dispersible and inhalable, and capable of killing 'superbugs' in the lungs of infected animals. For the time being, our study provides promising formulation and pharmacological information on inhalation delivery for fast-tracking translational research into new therapy.

4. Inhaled Nucleic Acid Therapeutics and Vaccines

Jenny Lam
Associate Professor
Department of Pharmacology and Pharmacy
The University of Hong Kong

BIOSKETCH

Dr Jenny Lam is currently Associate Professor in the Department of Pharmacology and Pharmacy, The University of Hong Kong. Dr Lam received her MPharm degree from The University of Nottingham (2001) and completed her PhD in drug delivery at the School of Pharmacy, The University of Nottingham (2006). Shortly afterwards, she was awarded the Maplethorpe Fellowship to continue her research in nucleic acid delivery in the Department of Pharmacy at King's College London. Since joining the University of Hong Kong in 2009, her research has focused on the development of novel delivery systems for macromolecular therapeutics, including nucleic acids, peptides and proteins, and the development of antimicrobial peptides against respiratory infections. She is also interested in spray drying and spray freeze drying technologies to produce inhaled powder formulation.

ABSTRACT

Various strategies exist to use nucleic acids, such as plasmid DNA, antisense oligonucleotides, small interfering RNA (siRNA) and microRNA (miRNA), to manipulate gene expression as a means to treat respiratory diseases such as cancer, lung infections and asthma. Moreover, nucleic acids such as DNA and messenger RNA (mRNA) can also be used as vaccines by encoding antigen to elicit a specific immune response. Exciting gene-editing platforms based on CRISPR have emerged as potential powerful therapeutics. These nucleic acid-based therapeutics have immense potential to treat diseases that are otherwise ‘undruggable’ with small drug molecules or other biologics. Nonetheless, their high molecular weight and highly negatively charged characteristic are at odds with the efficiency of transit various epithelial/endothelial barriers to reach their target sites. The objective of this presentation is 3-fold: (1) to describe the barriers to pulmonary nucleic acid delivery and how they may be overcome through delivery system design; (2) to describe peptide based delivery system for pulmonary nucleic acid delivery; and (3) to report on the use of spray drying and spray freeze drying technologies to produce highly dispersed powder formulation of nucleic acid for inhalation.

5. Polymeric Nanocapsules for Loading and Delivery of Naturally Occurring Agents for Tumor Therapy *in vitro* and *in vivo*

Khuloud T. Al-Jamal
Professor in Nanomedicine
Chair of Drug Delivery & Nanomedicine
Institute of Pharmaceutical Science
Faculty of Life Sciences and Medicine
King's College London

BIOSKETCH

Professor Khuloud T. Al-Jamal is a Chair of Drug Delivery & Nanomedicine, King's College London. She started her academic career as a lecturer at King's College London in 2011.

She is also a registered pharmacist at the General Pharmaceutical Council. She has completed her pre-registration pharmacy training at The University College London Hospital and was awarded the Overseas Research Award Scheme (ORSA) Scholarship from The University of London (2000-2004) to complete her PhD in Drug Delivery from The School of Pharmacy, University of London (currently known as UCL-School of Pharmacy).

She was awarded the prestigious CW Maplethorpe Research and Teaching Postdoctoral Fellowship from The University of London (2005-2007) to explore the use of cationic dendrimers as anti-angiogenic agents for growth inhibition of solid and metastatic tumours.

She has developed an extensive experience in designing and developing novel nanoscale delivery systems including dendrimers, liposomes, quantum Dots (QDs), polymers, viral vectors, chemically functionalised carbon nanotubes and graphene oxide. Her current work involves pre-clinical translation of novel nanomaterials designed specifically for drug, protein, nucleic acids and radionuclide delivery for therapeutic or diagnostic applications.

She was awarded and is managing a number of research projects funded by The Royal Society, Worldwide Cancer Research, EPSRC, BBSRC, FP6, FP7 and ITN Marie Curie research programmes. In February 2012, she was awarded the BBSRC New Investigator award exploring the use of chemically functionalised carbon nano-needles as vectors for delivering therapeutics across the BBB. In 2012, she was awarded the prestigious Royal Pharmaceutical Society Science Award in recognition for her outstanding scientific achievements in the field of Nanomedicine. She is a three-time winner of the Wellcome Trust Image Award (2014-2016).

ABSTRACT

Clinical applications of naturally occurring substances such as curcumin, quercetin and glabrescione B for the treatment of cancer and other chronic diseases have been hindered by their short biological half-lives and/or poor water solubility. Nanotechnology-based drug delivery systems have the potential to enhance the efficacy of poorly soluble drugs for systemic delivery. Our recent work has focused on the use of poly(lactic-co-glycolic acid) (PLGA)-based polymeric oil-cored nanocapsules (NCs) for high loading and delivery of such agents to different types of cancer, e.g., ovarian, colon and brain cancer in mice after systemic injection, with promising results obtained so far.

Formulations of different oil compositions were prepared and characterised for their drug loading, physico-chemical properties, and shelf-life stability. The results indicated that castor oil-cored PLGA-based NC achieved high drug loading efficiency (≈18% w(drug)/w(polymer)%) compared to other oil-cored NCs. Curcumin-loaded NCs, for example, internalised more efficiently in CT26 cells than the free drug, and exert therapeutic activity in vitro, leading to apoptosis and blocking the cell cycle. In addition, the formulated NC exhibited an extended blood circulation profile compared to the non-PEGylated NC, and accumulated in the subcutaneous CT26-tumors in mice, after systemic administration.

Thanks to live imaging techniques, optical and single photon emission computed tomography/computed tomography (SPECT/CT), which also confirmed tumour accumulation of these carriers. In vivo growth delay studies were performed, and significantly smaller tumour volumes were achieved compared to empty NC injected animals, in case of curcumin. Such studies showed the potential of polymeric NC for delivery and solving some physico-chemical problems encountered in the field of natural drugs.

6. Continuous Manufacturing – A strategy to Make High Pharmaceutical Quality Affordable

Ajaz S. Hussain
Principal, Insight, Advice & Solutions LLC
President, The National Institute for Pharmaceutical Technology and Education (NIPTE)

BIOSKETCH

Dr. Hussain distributes time between his consulting practice (http://www.ajazhussain.com/) and his role as President of the National Institute of Pharmaceutical Technology and Education (http://www.nipte.org/). He trained as a pharmacist at the Bombay College of Pharmacy, India; and received his Doctoral degree from the University of Cincinnati. His career path is diverse – academician, US FDA regulator, senior executive (in pharma and tobacco sector) and now an advisor and consultant with support for academia. He is passionate about making high pharmaceutical quality affordable and shares his view on the topic around the world and on his LinkedIn page (https://www.linkedin.com/in/ajazshussain).

ABSTRACT

For over two decades the US FDA has sought to reform its regulatory process to achieve *"a maximally efficient, agile, flexible pharmaceutical manufacturing sector that reliably produces high-quality drugs without extensive regulatory oversight."* This presentation will share insights on questions such as - Why is the US FDA seeking to improve the performance of pharmaceutical manufacturing? How does it plan to achieve this vision? What role will continuous production play in realizing this vision? Following this, the journey ahead will be described based on current challenges faced by industry and FDA to implement science-based performance standards to ensure optimal quality risk mitigation.

7. Next-Generation Biomanufacturing

Arthur C. Hewig
Director of Drug Substance Process Development
Amgen Inc.

BIOSKETCH

Art Hewig is a Director of Process Development at Amgen where he leads an integrated group that is designed to deliver end-to-end drug substance processes that robustly transfer to Amgen's commercial network. Prior to the role Art was heading Purification Process Development at Amgen. Art has been with Amgen since 2002, where his initial focus was developing purification processes for early and late stage molecules. During this time he developed and implemented real time PAT technologies utilizing light scattering and as well as connected downstream processing. Art holds a PhD in Chemical Engineering from Carnegie Mellon University.

ABSTRACT

Biomanufacturing change has been more evolutionary than revolutionary in comparison to other industries. Recent changes in the biopharmaceutical business landscape require agility, modularity, and dematerialization of manufacturing networks. This is essential for maintaining a biology-first modality independent approach in the development of Amgen's portfolio, which in the last few years has grown from a primarily monoclonal antibody and recombinant protein portfolio to one that is now comprised of over 10 molecule modalities. To overcome this challenge, Amgen is applying next generation manufacturing technologies and transitioning from a large fixed stainless steel network to a flexible biomanufacturing network optimized for speed and cost that seamlessly delivers to the multi-modal product portfolio. This presentation will cover the transformation of Amgen's network, describe the benefits realized, and discuss the continued revolution of next-generation manufacturing at Amgen.

8. Interchangeability, Who Decides?: Stakeholders, Regional Perspectives and Principles

Thomas Felix
Medical Director, R&D Policy
Amgen Inc.

BIOSKETCH

Dr Thomas Felix is a Medical Director, R&D Policy in Amgen's Global Regulatory Affairs and Safety organization. He has been at Amgen since 2006 and is currently based in Washington, DC, USA.

Dr. Felix serves in a technical policy role in North America, Asia, Western Europe, Latin America, and the Middle East. He has experience working in medical affairs on both small molecule and biologic therapeutics. Dr Felix contributes to a cross-functional, global multidisciplinary team committed to advancing science, policy and manufacturer accountability for a successful, patient-focused biosimilar implementation. He also works to advance pharmacovigilance (PV) systems to more accurately identify adverse events and associated manufacturers in a timely manner, including evolving adverse event traceability capabilities for multisource biologics in various treatment settings and regions. Dr. Felix also serves as a subject matter expert, informing U.S. state governments on necessary legislative provisions to allow for science-based substitution of biosimilars in the retail pharmacy setting. He represents Amgen as a corporate member to the following organizations: American Medical Informatics Association (AMIA), National Patient Safety Foundation (NPSF), and the Pharmacy HIT Collaborative. In 2017, he will serve a second year as the Vice-Chair to AMIA's Industry Advisory Council (IAC) and as a member of AMIA's Public Policy Committee. He also serves as Amgen's representative on the Academy of Managed Care Pharmacy's Biologics & Biosimilars Collective Intelligence Consortium (AMCP BBCIC) Planning Committee. He also has interests in advancing policy in the areas of patient preference inclusion in drug development, risk management and drug traceability.

Dr. Felix earned his medical degree at the PSG Institute of Medical Sciences and Research (India). Prior to Amgen, Dr. Felix was Vice President of Medical Affairs at an NBC Universal health media company (Healthology, Inc., New York, NY, USA), an organization dedicated to the development of physician-led educational programs on disease management across therapeutic areas.

ABSTRACT

The scientific differences between small molecule generics and large molecule biosimilars have required separate legal and regulatory frameworks for their approval and post-approval requirements around the world. It is generally agreed that biosimilars will not be substitutable in a manner often seen with generics. The terms of use for biosimilars is a current topic, but does not have a globally agreed nomenclature with some terms used very differently across regions. This session will cover the terms used around the world (i.e., substitution, switching, and interchangeability) and clarify their meaning in different jurisdictions. Criteria for assessment and principles for implementation to allow for multiple switches back and forth between a biosimilar and reference product will be presented.

9. Regulation of Drugs, Devices, and Gene and Advanced Cell Therapy in Japan

Mitsuru Hashida
Professor / Administrative Director
Institute for Integrated Cell and Material Sciences
Kyoto University Institute for Advanced Research

BIOSKETCH

Mitsuru Hashida received his Ph.D. degree from the Graduate School of Pharmaceutical Sciences, Kyoto University in 1979 and returned to its faculty member following postdoctoral fellowship at the University of Kansas. His research interests are focused on design and development of delivery systems for drugs, proteins, and gene medicines, and he is the author or co-author of 480 original articles. He was the recipient of Pharmaceutical Society of Japan Award, Controlled Release Society Founders' Award, and American Association of Pharmaceutical Scientists Research Achievement Award. He is currently serving as Chairman of the Pharmaceutical Affairs and Food Sanitation Council, Ministry of Health, Labor, and Wealth, Japan.

ABSTRACT

Regulation of pharmaceuticals, medical devices, and regenerative medicine is empowered by the Law on Securing Quality, Efficacy and Safety of Products including Pharmaceuticals and Medical Devices (PMD Act). Final approval of new products is granted by the Pharmaceutical Affairs and Food Sanitation Council (PAFSC), which serves as an advisory body to the Ministry of Health, Labour and Welfare (MHLW), and reviews and discusses important pharmaceutical and food sanitation-related matters in Japan. In the past few years, various new pharmaceuticals, medical device, and regenerative therapy products such as immune check-point inhibitor antibody, robotic medical device, and cell sheet for therapy of cardiac insufficiency have become used in clinical practice. In order to support these progresses, various projects for creating new guidelines, etc. are carried out in parallel. Establishment of new systems for accelerating development such as those similar to Fast track designation, Breakthrough therapy designation, and Priority review designation is also an important issues in pharmaceutical affairs in Japan. We should pay the attention to the progress of basic sciences, such as nanomedicine, molecular imaging of biological process, and computation and MEMS (Micro-Electro Mechanical Systems) technology, in support of innovation of medicine. In this presentation, outline of the regulatory system in Japan would be reported, and the recent achievement of our study on development of new drug delivery systems will be described be discussed.

10. Data Mining and Visualization Techniques for ADME Screening in Early Drug Discovery

Fumiyoshi Yamashita
Professor
Graduate School of Pharmaceutical Sciences
Kyoto University

BIOSKETCH

Dr. Yamashita is Professor of Graduate School of Pharmaceutical Sciences, Kyoto University, Kyoto, Japan. He received his B.S. (1987), M.S. (1990), and Ph.D. in Pharmaceutical Sciences (1995) from Kyoto University, respectively. He was appointed Research Assistant Professor of Faculty of Pharmaceutical Sciences, Kyoto University in 1992. From 1995 to 1996, he was a visiting scientist of School of Pharmacy, University of Southern California, Los Angeles, California. He was appointed Associate Professor of Graduate School of Pharmaceutical Sciences, Kyoto University in 1996, and promoted to Professor in 2016.

ABSTRACT

ADME properties relate to efficacy and safety of a drug and are crucial to the final clinical success of a drug candidate. A rational approach to increase the efficiency of pharmaceutical R&D is to reduce the attrition rate in the costly downstream stages by increasing the attrition rate in the less costly, earlier stages of the process. In vitro experimental ADME assays have been developed to meet the challenges of a large number of compounds and shortened cycle time. Although the throughput of simplified in vitro ADME assays was greatly improved than ever before, random screening remains still costly and time-consuming. To uncover trends and patterns of acquired data assists drug design and research of novel drug candidates. Structure-activity relationship (SAR) analysis is the process of finding the relationship between chemical structure of a molecule and its biological property, which comprises molecular descriptors computation and stochastic input-output modeling. To enable better predictability, machine learning approaches including artificial neural network and genetic algorithm have also been introduced. On the other hand, readability of SAR models should be taken into account to ensure usefulness for drug design. In addition to SAR modeling methods for ADME properties, we have developed large-scale data visualization techniques for providing intuitive understanding of SAR relationship. This presentation will discuss the effectiveness of modeling and visualization for ADME properties.

11. Herb-drug Interactions: Impact in Therapeutic Outcome of Integrative Medicine

Joan Zuo
Director and Professor
School of Pharmacy
The Chinese University of Hong Kong

BIOSKETCH

Professor Joan Zuo is the Director and Professor of the School of Pharmacy at the Chinese University of Hong Kong. She holds a B.Sc. and a Ph.D. in Pharmaceutical Sciences and has had over 20 years' experience in the biopharmaceutics and pharmacokinetics fields. Since joining the School of Pharmacy at CUHK in January 2000, Prof. Zuo has secured over HK$13 million competitive extramural funding to support her research. Her research focus has been on quality control and delivery of western drugs and herbal products, as well as elucidation and prediction of potential herb/drug interactions in patients. She has over 200 original research and conference papers and several patents in USA, China, Hong Kong and Malaysia. In Hong Kong, Prof. Zuo is serving in the *Pharmacy & Poison's Board*, *Pharmacovigilance Committee*, *TCM Research and Development Committee* and *Proprietary Traditional Chinese Medicine Registration Committee* at the government of Hong Kong Special Administration Region, China. Internationally, Prof. Zuo has served as nomination committee member for *International Society of Xenobiotics (ISSX)* and is currently the editorial board member for *Biopharmaceutics and Drug Dispositions, Xenobiotica, Chinese Medicine* and, grant reviewer for China and Macau, and journal reviewer for more than 50 international peer reviewed journals.

ABSTRACT

The introduction of Integrative Medicine in Hong Kong's healthcare system has facilitated the development of innovative models that provide patients with the medicine they needed. In 2014, Hospital Authority initiates two pilot projects on stroke rehabilitation and cancer palliative care. In order to ensure the safety as well as the effectiveness of therapy, studies on the potential herb/TCM-drug interactions are essential. After more than a decade-long of successes in unravelling the mystery of absorption, metabolism and disposition of herbal active marker compounds following oral administration, our research group has made a strategic move to set up a comprehensive platform for investigation of herb-drug interactions. In the current talk, our herb-drug interaction researches experiences in the fields of preclinical, clinical as well as systematic review will be highlighted. Examples on the systematic research on the herb-drug interaction between Radix Salvia miltiorrhiza (Danshen) and Radix Puerariae lobatae (Gegen) during anti-coagulation therapy will be demonstrated. In addition, the challenges in the herb-drug interaction researches will be discussed.

12. Translation of Orphan Disease Trial Design into General Drug Development

E. Dennis Bashaw
Director
Division of Clinical Pharmacology-3
Office of Clinical Pharmacology
U.S. Food and Drug Administration

BIOSKETCH

Dr. Bashaw received his BS and Doctor of Pharmacy from the University of Kentucky in 1986. Following a residency at the National Institutes of Health, he accepted a commission in the United States Public Health Service as a reviewer at the FDA in 1987. He was appointed Director of the Division of Clinical Pharmacology-3 in 2006 and currently oversees the work of 28 PhDs. and PharmDs. The Division has the primary Clinical Pharmacology review responsibility for the areas of:

- Gastrointestinal and In-Born Errors of Metabolism
- Bone, Reproductive and Urologic Drugs
- Dermatology and Dental Drug Products

ABSTRACT

The “gold standard” for drug evaluation has been, since the 1970s, the replicate clinical trial (RCT). As such it provides a high degree of certainty with regards to therapeutic response and, when sized properly, provides an assurance with regards to the delineation of adverse effects. For the rare disease population, where patient numbers are constrained, the RCT paradigm has given way to new approaches using either a single clinical trial with supportive data in the form of biomarkers or other non-traditional study designs up to and including the N of 1 trial. The use of such designs is being further accelerated by the establishment of accelerated development approaches by regulatory agencies. The utility of such innovative approaches is more and more being applied to “mainstream” drug development and is providing a pathway to both cost-savings and in more clinically relevant “patient-centric” drug development. This is a direct outgrowth of both the evolution of Clinical Pharmacology tools and our application of them to what was a traditionally underserved population. The presentation will provide an overview of the traditional RCT paradigm and its evolution as “the gold standard” and how the challenges encountered in the Orphan Drug/Rare Disease environment have challenged our assumptions and ultimately driven innovation in clinical trial design.