香港中文大學
The Chinese University of 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

School of Pharmacy CUHK
Expanding the pharmaceutical universe,
Creating opportunities for life

School of Pharmacy
Faculty of Medicine
The Chinese University of Hong Kong

Workshop in Celebration of 25th Anniversary of the School of Pharmacy

Biopharmaceutics of Modified Release Products and Challenging Drug Molecules

16 JULY 2016 SATURDAY

9AM – 6PM

LT3, YIA, CUHK

This workshop is equivalent to 2 CEU points

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Dear Colleagues,

On the eve of its 25th anniversary, it is gratifying to take stock on the impact this pioneering pharmacy school has made in tertiary education in Hong Kong. In rapid succession since the introduction of the BPharm program in 1992, the school launched an M.Phil and a PhD program to train research scientists, and shortly thereafter a MCP self-financed program to train clinical pharmacists. More recently in 2012, it launched the PMQ self-financed program to answer government's mandate to upgrade the quality of the drug products manufactured locally. Also in 2012, the School took a bold step to compete for additional funding to bring about an increase in BPharm student intake from 30 to 60. It was reasoned that with more pharmacists in place to take care of the dispensing function, pharmacists with the aptitude and advanced training will then be able to practice pharmacy at a higher level. This is what would be expected of pharmacy practice in an advanced economy like that in Hong Kong.

Under the leadership of Professor Moses Chow, former Director of the CHUK School of Pharmacy, the school developed expertise in conducting bioavailability/bioequivalence studies on drug products manufactured locally that were competing for tender in the Hospital Authority. This one-day workshop was organized to provide everyone with foundation knowledge on this important subject of assuring drug product quality. The School intends to organize future forums that will bring the regulators and the trade under one roof to discuss innovative ideas of regulatory importance and mutual benefit.

The School is now on the threshold of a second act to demonstrate its resolve in masterminding thematic research around an area that will differentiate CUHK School of Pharmacy on campus as well as among its peers. This would require transforming the research culture in the school and refining the role of teachers as facilitators of learning; creating a renewed emphasis on creativity, discovery, and research; and establishing a critical mass to build a world class research program. World leading research or research that is internationally excellent is absolutely necessary for the School of Pharmacy to realize its vision "to be a prestigious school of pharmacy in the Pacific Rim dedicated to advancing research and education in the creation of affordable innovative medicine."

I hope this message has provided you with a glimpse of the school's past accomplishments and its plans for the next decade.

I hope you enjoy today's workshop.

Sincerely,

Vincent H.L. Lee
Research Professor
School of Pharmacy
Faculty of Medicine
The Chinese University of Hong Kong

Contents

Programme

MORNING SESSION (9:00a.m. – 12:15p.m.)

9:00a.m.	**Opening Remarks** ***Joan ZUO*** *School of Pharmacy, The Chinese University of Hong Kong* ***Linda WOO*** *Drug Office, Department of Health* ***Vincent LEE*** *School of Pharmacy, The Chinese University of Hong Kong*	**Moderator** ***Vincent LEE*** *Research Professor* *School of Pharmacy, CUHK*
9:15a.m.	**Implementation of BABE Requirements at the FDA: Lessons Learned** ***Vinod P. SHAH*** *Pharmaceutical Consultant*	
10:10a.m.	**Immediate Release and Modified Release Bioequivalence Requirements** ***Vinod P. SHAH*** *Pharmaceutical Consultant*	
11:10a.m.	**Break**	
11:15a.m.	**Regulatory Assessment of Critical Dose/NTR Drugs in Hong Kong** ***Clive CHAN*** *Drug Office, Department of Health*	
12:10p.m.	**Lunch** *(Onsite Complimentary)*	

AFTERNOON SESSION (1:00p.m. – 6:00p.m.)

1:00p.m.	**Modified Release: Formulation Design & Drug Release Mechanisms** ***Thomas LEE*** *School of Pharmacy, The Chinese University of Hong Kong*	**Moderator** ***Joan ZUO*** *Director and Professor* *School of Pharmacy, CUHK*
1:50p.m.	**Biowaivers: BCS and IVIVC** ***Vinod P. SHAH*** *Pharmaceutical Consultant*	
2:50p.m.	**Combination Products: A Simulation Study of BABE** ***Teddy LAM*** *School of Pharmacy, The Chinese University of Hong Kong*	
3:50p.m.	**Break**	
4:00p.m.	**Design and Regulatory Assessment of Transdermal Drug Products** ***Vinod P. SHAH*** *Pharmaceutical Consultant*	
5:00p.m.	**Regulatory Assessment of Biosimilars in Hong Kong** ***Clive CHAN*** *Drug Office, Department of Health*	
6:00p.m.	**Open Forum**	

BIOGRAPHIES

Vinod P. SHAH

Pharmaceutical Consultant

Dr. Shah is a pharmaceutical consultant. He was Scientific Secretary (2003 – 2011) of International Pharmaceutical Federation (FIP), and is now Chair of Regulatory Sciences Special Interest Group of FIP. He is a member of steering committee of Non-Biological Complex Drugs (NBCD) and a Board Member of Product Quality Research Institute.

Dr. Shah retired from US FDA (Food and Drug Administration) as a Senior Research Scientist after 30 years of service in July 2005. At FDA, he has developed several Regulatory Guidances for Pharmaceutical Industry in the area of dissolution, SUPAC, bioequivalence and biopharmaceutics. He has received several FDA Awards including Award of Merit, Scientific Achievement Award and Distinguished Career Service Award.

Dr. Shah is author/co-author of over 300 scientific papers and is a co-editor of four books. Dr. Shah was the President of American Association of Pharmaceutical Scientist (AAPS) in 2003. He is a Fellow of AAPS and FIP. Dr. Shah is a recipient of AAPS Distinguished Service Award, Pharmaceutical Sciences World Congress (PSWC) Research Achievement Award, FIP Lifetime Achievement Award in Pharmaceutical Sciences and Honorary Doctorate from Semmelweis University, Hungary.

Clive CHAN

Senior pharmacist
Drug Office
Department of Health

Mr. Clive Chan is the senior pharmacist of the Department of Health Drug Office Drug Registration Unit, and is also the secretary of the Pharmacy and Poisons (Registration of Pharmaceutical Products and Substances: Certification of Clinical Trial / Medicinal Test) Committee established under the Pharmacy and Poisons Board.

Mr. Chan finished his bachelor degree of pharmacy in the University of Wales Institute of Science and Technology, bachelor degree of law in the Manchester Metropolitan University, and master degree of medical sciences in the University of Hong Kong.

Currently, Mr. Chan is responsible in the pre-approval evaluation of applications for registration of pharmaceutical products. Previously, he was the senior pharmacist in the Drug Registration Unit responsible in the post-approval evaluation of applications for change of registered particulars of registered pharmaceutical products, and in the Pharmacovigilance Unit responsible in the monitoring of the safety of medicines.

Thomas LEE
Assistant Professor
School of Pharmacy
Faculty of Medicine
The Chinese University of Hong Kong

Dr. Thomas Lee joined the School of Pharmacy at the CUHK in 2013. He graduated with B.Pharm. (Hons) Degree from the formerly Department of Pharmacy at the CUHK and received his Ph.D. in Pharmaceutical Sciences (Drug Delivery) from the University of Wisconsin-Madison in USA. Before joining the School of Pharmacy, Dr. Lee spent a decade in two multinational pharmaceutical companies. After almost 6 years at Novartis Pharmaceuticals Corporation, he was recruited to Celgene Corporation to serve as a manager of the Formulations R&D.

Biopharmaceutics of Modified Release Products and Challenging Drug Molecules

Teddy LAM

Assistant Professor
School of Pharmacy
Faculty of Medicine
The Chinese University of Hong Kong

Dr. Teddy Lam joined the School of Pharmacy at the Chinese University of Hong Kong in 2011. He graduated with Pharm.D. and Ph.D. degrees from School of Pharmacy, University of California, San Francisco. Before joining CUHK, Teddy had six years of in-patient pharmacy practice experience in medical centers of Kaiser Permanente Northern California. His primary research focuses on using modeling and simulation to gain mechanistic insights from existing pharmacokinetic data. His research interests encompass both traditional, pharmacometric analyses and newer, multi-level, agent-based, discrete-event models and simulations. Present research activities include building and using agent-based pharmacokinetic models and simulations to represent human drug absorption in bioavailability/bioequivalence studies, to study the phenomenon of transporter-enzyme interplay, and to represent *in vitro* pharmacokinetics and disposition of baicalein flavonoids. In addition, in collaboration with the Stanley Ho Centre of Emerging and Infectious Diseases and Princess Margaret Hospital, he is currently conducting a clinical trial to demonstrate the efficacy and safety of genotype-based low dose efavirenz in treating local Chinese HIV-positive patients.

ABSTRACTS
MORNING SESSION

Implementation of BABE Requirements at the FDA: Lessons Learned

Vinod P. SHAH
Pharmaceutical Consultant

Abstract

The mission of a regulatory authority is to assure that safe and effective drugs are marketed in the country and are available to the people. FDA ensures that the generic drug products are safe and effective, are pharmaceutically equivalent and bioequivalent to the brand-name counterparts – the same dose of the same active ingredient, delivered in the same way, and manufactured according to the same standards of quality. The quality of the product is ensured thru product identity, strength, purity, assay, potency, content uniformity, dissolution (for solid oral dosage forms) and being manufactured under FDA's good manufacturing practice. Additionally, it monitors the process thru compliance activities, analysis and encouraging every pharmaceutical company's goal to include "Quality".

Immediate Release and Modified Release Bioequivalence Requirements

Vinod P. SHAH
Pharmaceutical Consultant

Abstract

IR Products:

A single dose fasted study comparing the highest strength of test and reference product is required. Food effect study is required if indicated in the labeling. In all cases, it must meet the BE criteria and *in vitro* drug release requirement.

MR Products:

A single dose fasted study comparing the highest strength of test and reference product is required. A multiple dost study is NOT required. A food-effect study comparing highest strength of Test and Reference Product is needed. In all cases, it must meet BE criteria and *in vitro* drug release requirements.

For both IR and MR products, the lower strengths can get biowaiver based on formulation proportionality and dissolution profile similarity.

The regulatory requirements are dynamic in nature, keep changing to meet new challenges. These will be addressed with examples.

Regulatory Assessment of Critical Dose/NTR Drugs in Hong Kong

Clive CHAN
Drug Office, Department of Health

Abstract

In April 2009, the Pharmacy and Poisons (Registration of Pharmaceutical Products and Substances: Certification of Clinical Trial/Medicinal Test) Committee of the Pharmacy and Poisons Board (the Board) decided that proof of bioequivalence for generic drugs known to have narrow therapeutic index should be required for the approvals of new and renewal applications for registration of pharmaceutical products, and implemented by phases according to their known hazards. In April 2010, the Phase 1 requirement for anti-epileptic drugs covering 29 drug substances was implemented accordingly.

In August 2013, the Board endorsed the decision to establish an Expert Advisory Group on BABE studies (the BABE Expert Group) to facilitate the implementation of the above requirement for new and renewal registration of generic drugs. The BABE Expert Group was chaired by the Assistant Director (Drug), with 11 local members from the academia, pharmaceutical trade, Hospital Authority, Department of Health, medical and pharmacy professions, as well as 2 overseas co-opted members.

In 2014 and 2015, the BABE Expert Group discussed and decided an implementation plan for the Phase 2 requirement covering a list of 38 drug substances regarded as Critical Dose Drugs / Narrow Therapeutic Range Drugs, subject to consultation with stakeholders on the proposed implementation timeline of one year after formal announcement of the Phase 2 requirement by the Board.

In August 2015, the Department of Health conducted 2 consultation sessions with the stakeholders, including members of the pharmaceutical trade associations and representatives of the clinical trial centres of the 2 local universities.

The Department of Health noted, and had conducted follow-up actions on the comments and concerns received from the consultation sessions, which included seeking comments from an overseas co-opted member, and reporting the findings of the consultation sessions and comments by the overseas co-opted member to the BABE Expert Group for endorsement on the refined implementation plan and timeline.

The Pharmacy and Poisons (Registration of Pharmaceutical Products and Substances: Certification of Clinical Trial/Medicinal Test) Committee will consider the refined implementation plan and timeline endorsed by the BABE Expert Group, and will inform the stakeholders on the development of the Phase 2 requirement for BABE studies accordingly.

ABSTRACTS
AFTERNOON SESSION

Modified Release: Formulation Design & Drug Release Mechanisms

Thomas LEE
School of Pharmacy, Faculty of Medicine
The Chinese University of Hong Kong

Abstract

Drug delivery research is currently at an exciting juncture. The major advances in controlled release technology, together with the dramatic increase in the knowledge of biopharmaceutics, pharmacokinetics and pharmacodynamics computer modeling, provide unprecedented opportunities to develop potentially useful treatments to meet the unmet medical needs.

I will provide an overview on controlled release technology, including the fundamental theories of controlled release as well as advantages and limitations of controlled release technology. Drug release mechanisms and practical considerations in the design of controlled release dosage forms will be also discussed.

Biowaivers: BCS and IVIVC

Vinod P. SHAH
Pharmaceutical Consultant

Abstract

The term biowaiver is applied to a regulatory drug approval process when the dossier (application) is approved based on evidence of equivalence other than *in vivo* bioequivalence test. For solid oral dosage forms, Biowaiver(s) is generally based on a dissolution test.

Biopharmaceutics Classification System:

Biopharmaceutics Classification System (BCS) is a framework for classifying drug substance based on its solubility and permeability. Drug products under BCS Class 1 and 3 are eligible for biowaiver if it meets appropriate dissolution test criteria when compared with the brand name (innovator) drug product. The scope and control of biowaiver criteria will be discussed.

***In Vitro - In Vivo* Correlation (IVIVC):**

It is a functional or qualitative relationship between *in vitro* dissolution and *in vivo* bioavailability parameters. Different levels of IVIVC, methods of determination and its impact will be discussed.

Biowaivers lower the regulatory burden; it provides regulatory relief without loss of drug product quality.

Combination Products: A Simulation Study of BABE

Teddy LAM
School of Pharmacy, Faculty of Medicine
The Chinese University of Hong Kong

Abstract

Fixed-dose combination medicinal products have been increasingly used due to the benefit of the combined effects of active substances given together. When used appropriately, fixed-dose combinations are more convenient and therefore may lead to better medication adherence. A typical combination is co-formulation of a primary active drug with its pharmacokinetic enhancer; examples of which include amoxicillin-clavulanate and carbidopa-levodopa.

In this presentation, I seek to evaluate the pharmacokinetic and pharmacodynamic consequences of altered absorption rate and extent of both the primary active drug and the pharmacokinetic enhancer, using carbidopa-levodopa combination for illustration. Simulations will be carried out with a simple pharmacokinetic-pharmcodynamic model to illustrate unusual scenarios like dose-dumping, prolonged release and potential food effect. Expected exposure and response profile will be examined.

Design and Regulatory Assessment of Transdermal Drug Products

Vinod P. SHAH
Pharmaceutical Consultant

Abstract

Transdermal drug products are applied topically for systemic action; the drug is absorbed through the skin into blood circulation and transported to target tissues to achieve therapeutic effect. The design and basic elements of transdermal drug products, its advantages and limitations will be discussed. Transdermal drug products are considered as new drug products. The regulatory requirements and tests needed for approval will also be discussed in detail.

Regulatory Assessment of Biosimilars in Hong Kong

Clive CHAN
Drug Office, Department of Health

Abstract

In Hong Kong, all pharmaceutical products must satisfy the criteria of safety, quality and efficacy, and must be registered with the Pharmacy and Poisons Board before they can be sold in the market. Pharmaceutical products may contain chemical or biological materials as active ingredients.

Biological products (i.e. pharmaceutical products containing biological materials as active ingredients) are distinguished from chemical products by being derived from living organisms and frequently having complex molecular structures. They require special quality consideration because of the biological nature of the starting materials, the manufacturing processes, and/or the test methods needed to characterize batches of the products.

The expirations of patent and/or data protection of the originator biological products have led, or will lead, to the development of copy versions of these products. In light of the special quality consideration with biological products, these copy versions cannot be considered as identical, but merely similar, to the originator products because of the inevitable differences in molecular structures and quality attributes arising from their different manufacturing processes. These copy versions of the originator products are commonly referred as biosimilar products.

In line with international practice and scientific consensus, the registration of biosimilar products cannot use the same approach of generics for chemical products, i.e. cannot reply on bioequivalence and quality data only. Safety and efficacy data in comparison with the originator products are also necessary. These requirements are included in the Guidance Notes for Registration of Biosimilar Products available on the Department of Health Drug Office website.

Acknowledgements

The School of Pharmacy of the Chinese University of Hong Kong gratefully acknowledges the workshop faculty in sharing their expert knowledge regarding regulatory challenges inherent in the biopharmaceutics of modified drug formulations and structurally complex drug molecules. In addition, the School wishes to recognize the staunch support of its partners in the health product industry in the form of sponsorships or educational grants. These resources enabled the School to engage Dr. Vinod Shah, a well-respected, influential pharmaceutical scientist who devoted 3 decades of his career at the U.S. Food and Drug Administration, to share his insights and experience on the role of bioavailability and bioequivalence in rendering decisions on the interchangeability of pharmaceutical drug products.

This one-day workshop is one of the several events in the School's celebration of its 25 years of partnership with the stakeholders in the pharmacy community in Hong Kong, particularly its graduates in all the degree programs pioneered by the School. The workshop faculty comprises Dr. Vinod Shah, Mr. Clive Chan, Professor Teddy Lam and Professor Thomas Lee.

The sponsors are:

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ENQUIRIES

Email	:	sop.med@pharmacy.cuhk.edu.hk
Telephone	:	(852) 3943 6831
Fax	:	(852) 2603 5295
Homepage	:	http://www.pharmacy.cuhk.edu.hk
Facebook	:	http://www.facebook.com/cuhk.pharmacy
Address	:	School of Pharmacy Faculty of Medicine 8th Floor, Lo Kwee-Seong Integrated Biomedical Sciences Building, Area 39, The Chinese University of Hong Kong, Shatin, New Territories, Hong Kong SAR