Product Workshop:

Pharmaceutical Aerosols

A Practical Introduction to the Technical Basics of Developing Inhaled Pharmaceutical Products

Hosted By:
Department of Pharmacology and Pharmacy
The University of Hong Kong

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MONASH University
Welcome

to the Pharmaceutical Aerosols Product Workshop

A Foundation Workshop affiliated to Inhalation Asia 2013

Asia is poised as a key market and frontier for inhaled product development. We are delighted in offering this Workshop that brings together for the first time, a unique collection of world-leading experts in Inhaled Product Development. The Team has been selected primarily because of their extensive industry and regulatory experience: their aim will be to share experiences of landmark past, current and future inhaled products, and provide a 2 day foundation course exposing scientists new to this field to key technical aspects of developing inhaled products.

The Workshop is hosted by University of Hong Kong in association with Inhalation Asia 2013 and the PDI Science Group: the first such regional conference to bring global inhalation science and technology to the Gateway of the world's most rapidly growing and evolving inhaled product market. The programme is coordinated by Dr. Philip Kwok and Associate Professor David Morton. David Morton brings extensive experience of running similar workshops in inhaled products, and for 10 years was Chair of Drug Delivery to the Lungs: the longest running annual international pulmonary delivery conference series.
The Workshop Programme

Monday 24 June 2013: University of Hong Kong

1.30pm Welcome and Introduction: [Prof Philip Kwok and Assoc Prof David Morton]

1.45pm Keynote Address: Current and Future trends in Inhalation Technology: [Prof E French, The University of Bath]

Part A: Fundamentals of Aerosol Science and Technology

2.45pm What is an aerosol, size distributions and moments, inertial properties of aerosols and lung transport/deposition [Dr P Kwok, The University of Hong Kong]

3.15-3.30pm Tea Break

4.00pm Understanding material science of powders as primary materials [Mr T Freeman, Freeman Technology]

Part B: Foundation- Generation of Aerosols from Medical Devices:

5.00pm Nebuliser/soft mist:
   - Outline of devices and formulation technologies [A. Prof. D Morton, Monash University]

5.45pm Review and Close of Day 1

Tuesday 25 June 2013: University of Hong Kong

Part B Continues: Foundation- Generation of Aerosols from Medical Devices:

9.00am pMDIs:
   - Outline of device and formulation technologies, mechanisms [Dr P Rogueda, Monash University]

10.00am DPIs:
   - Outline of devices and operation [Dr J Tibbatts, Concept Flow]
   - Formulation technologies and mechanisms [Dr J Shur, University of Bath]

11.30am Coffee/Tea

Part C: Measurement of the Aerosol Cloud

11.45am Compendial in vitro methods for Uniformity of Delivered Dose and Aerodynamic Particle Size Measurement (Impactors and Impingers) [Mr M Copley, Copley Scientific]

12.45pm Lunch and Exhibition

2.15pm Testing protocols, stability issues, data requirements [Mr J Parks, GSK Australia]

3:00pm Laser diffraction particle sizing and the practical applications and issues for measuring inhaler powders, sprays and finished product systems [Dr. Ulrich Kesten, Sympatec GmbH]

Part D: Outline of Regulatory and Safety Aspects for Inhalation Products

3.45pm: Tea/Coffee

4.00pm Keynote Address: Commercialisation of Regional Inhalation Products and Opportunities [Prof H K Chan, University of Sydney, Prof. Dr A Bhome ICOLD, ANOLD]

5.30pm Workshop Review

6.00pm Workshop Close
SESSION 1: Keynote Address - Current and Future trends in Inhalation Technology

Professor Edward French

SESSION ABSTRACT: The technological developments in inhalation are being driven largely by market place and by unmet medical need. However, this statement means very different things in different scenarios. Where to the developed medical economies, unmet medical need is the provision of new therapies for COPD and acute asthma exacerbations. In resource poor settings, amongst the developing economies (a potentially huge market), the provision of basic single agent bronchodilator or steroid therapy is a key medical and economic challenge. In addition, new technologies and techniques are also in development to facilitate simpler routes for development of new and existing drugs to hit these unmet needs. This talk will outline the key drivers for current technology development, what is being done currently to meet the market and scientific need and what is in the pipeline to come.

BIO: Eddie French is currently the Consultant Director of Biopharmaceutical Development of the Research in Medicines Design (ReMedDes) Group in the Department of Pharmacy and Pharmacology at the University of Bath, UK, and an independent pharmaceutical consultant. Prior to this Eddie worked for Pfizer World Wide R&D for 17 years in Pharmaceutical formulation design and development. He spent the last 8 years of his career at Pfizer as a director in the Inhalation and Devices Centre of Emphasis, focusing on the development of dry powder inhaler formulations and devices. This included 18 months as the technical lead for the second generation inhaler for Pfizer's Exubera™ (inhaled insulin). Eddie was previously chair of the Academy of Pharmaceutical Sciences of Great Britain, and currently leads the inhalation focus group of that organization. Eddie is a visiting professor of pharmaceutical science at Bath and the special professor of formulation science at the University of Nottingham. Any spare time he has is spent in the gym, watching rugby or playing touch rugby.

SESSION 2: Basics of Aerosol Particles

Dr. Philip Kwok

SESSION ABSTRACT: Drugs have been delivered to the lungs since ancient times for recreational and medical purposes. The lungs are an ideal site of administration for the treatment of local and systemic diseases. Inhalation is non-invasive, provides rapid onset of action, reduces the dose, and avoids first-pass metabolism by the liver. Drugs must be in the form of aerosols in order to be inhaled. Aerosols are suspensions of solid or liquid droplets suspended in a gas. Particle sizes range from nanometres to micrometres. Factors that can affect particle deposition in the lungs include particle size, shape, surface roughness, and electrostatic charge. The disease state, geometry of the respiratory tract, breathing patterns, and humidity can also influence deposition. Aerodynamic diameter is the most commonly used equivalent diameter to describe the size of aerosolised particles. The aerodynamic diameter range for optimal pulmonary drug delivery is 0.5 – 5 μm. Particles of these sizes are generally cohesive, causing poor flowability and dispersibility. Various formulation strategies to reduce the cohesion may be employed to improve the aerosolisation performance.
SESSION: 3: Understanding material science of powders as primary materials

Mr. Tim Freeman

SESSION ABSTRACT: Powders have been utilised by mankind for many thousands of years, and yet a great deal about their behaviour remains poorly understood. In contrast to liquids and gases, our ability to predict behaviour by employing a purely mathematical approach remains a work in progress. Yet the powder processing industry confronts challenges on a daily basis relating to product development and formulation, process scale-up, commercial manufacture, changes of raw material supplier, migrating from batch to continuous, etc. There is no shortage of examples where powder behaviour has a fundamental influence on the success or failure of a process or application and a wide range of different behavioural characteristics of a powder will be important at various stages. This session will demonstrate how the properties of a formulation need to be optimised to suit an application and, in the case of inhalation devices, meet the specific requirements and functionality of the delivery method employed whether the finished product is a blister, capsule or reservoir.

BIO: Tim Freeman is Managing Director of powder characterisation company Freeman Technology for whom he has worked since the mid 1990s. He was instrumental in the original design and continuing development of the FT4 Powder Rheometer and in the past decade has co-led the team that has grown Freeman Technology from a start-up business to the global organisation of today. Through his work with various professional bodies and involvement in industry initiatives Tim is an established contributor to wider developments in powder processing.

Tim has a degree in Mechatronics from the University of Sussex in the UK. He has extensive experience in application and method development for the FT4 Powder Rheometer and works closely with customers worldwide across the powder processing industries. Tim is a mentor on a number of project groups for the Engineering Research Center for Structured Organic Particulate Systems in the US http://ercforsops.org. He is a frequent contributor to industry conferences, instructs on training courses for powder processing and writes regularly for a variety of publications.

In the pharmaceutical field Tim is a past Chair of the American Association of Pharmaceutical Scientists (AAPS) Process Analytical Technology Focus Group and is a member of the Editorial Advisory Boards of Life Science Leader magazine (Jameson Publishing Inc. http://www.lifescienceleader.com) and Pharmaceutical Technology (Advanstar Communications Inc. www.pharmtech.com)
SESSION ABSTRACT: This presentation will introduce the basic types and operation of medical nebulisers. Nebulisers have been delivering medication to the lung for centuries. Compared to powder dispersion, the basic processes of liquid atomisation are better understood. This better mechanistic understanding results from spray behavior in fields varying from fuel injection to instrument design, printers to spray dryers. The result of this knowledge is in recent years a growing number of new, stand-alone, liquid-atomizing inhaler devices.

BIO: Dr David Morton is Associate Professor at the Monash Institute of Pharmaceutical Science, within Monash University, Australia.

David gained his BSc and PhD in chemistry from Bristol University, UK. From 1990, he worked at AEA Technology, initially studying aerosol generation, transport and leakage behaviour in the context of nuclear accidents. He then extended this work into developing new techniques for generating aerosol-based powders and nanoparticles for use in advanced materials applications, such as phosphors, superconductors and technical ceramics.

In 1997, David joined the Centre for Drug Formulation Studies at the University of Bath to manage their industry-funded dry powder inhaler product development programmes. In 1999, this group spun out into the drug delivery company Vectura Group plc, where David was Head of Pulmonary Research, and responsible for developing Vectura’s inhalation technology platforms. During this time, he was responsible for devising the PowderHale formulation technologies, and worked extensively on optimising powder-device combinations. Of the notable achievements have been associated technology licensing agreements in excess of US$400M, and has contributed to several inhaled products now on the market, or in late phase development.

David was co-chair of the “Drug Delivery to the Lung” international conference series for over 10 years.

In 2007, David left the UK to take up the position at Monash University, with specific research interests in particle engineering, drug delivery and particle surface modification. Most recently, he has led the creation of a partnership with GSK: a $3.5m Centre of Pharmaceutical Innovation and Industrialisation, which is seen as unique and a model for future industry-research institute collaborations.

David has authored over 35 patent applications, and despite his industrial career has over 75 peer reviewed publications, and 100 conference papers.
SESSION 5: pMDIs Outline of device and formulation technologies, mechanisms

**Doctor Philippe Rogueda**

BIO: Director of Emerging Technologies at Actavis. An industry-renowned Product Development Specialist with extensive experience of formulation science and device technologies working within global blue chip organisations. Areas of expertise include: driving innovative drug delivery from initial concept through to product development in oral and inhaled technologies through sPoC to Phase III; creating innovative research techniques, adapting technologies from alternative industry sectors; and utilising personal international network to drive commercial success.

SESSION 6: DPIs Outline of devices and Operation

**Doctor James Tibbatts**

BIO: Managing Director, Concept Flow. Medical Device innovation, research, technology development, IP, and product development/design engineering.

SESSION 7: DPIs Formulation technologies and mechanisms

**Doctor Jag Shur**

BIO: Director of Technology and Operations at Nanopharm Ltd. University of Bath.
SESSION 8: Compendial in vitro methods for Uniformity of Delivered Dose and Aerodynamic Particle Size Measurement (Impactors and Impingers)

Mr Mark Copley

SESSION ABSTRACT: This presentation will cover current USP and Ph.Eur. based in-vitro testing methods for MDIs, DPIs and Nebulizers, to include Delivered Dose Uniformity (DDU) and Aerodynamic Particle Size Distribution Measurements (APSD) by Cascade Impaction, concentrating on how the tests differ between inhaled product types. It will also focus on system suitability and validation considerations, and also look at ways to troubleshoot.

BIO: Mark Copley graduated from the University of Bath, UK in 2000 with a Masters Degree in Aerospace Engineering. For 8 years he was Technical Sales Manager and product specialist for Copley Scientific’s range of inhaler testing equipment and is now Sales Director for the company. Mark is considered a leading authority in testing methods and systems for metered-dose inhalers, dry powder inhalers, nebulisers and nasal sprays; authoring and contributing to more than 30 published articles. He also provides application support and consultancy, runs focused training workshops for the inhaled drug testing sector of the pharmaceutical industry and sits on the editorial advisory panel of Inhalation Magazine. An invited member of the European Pharmaceutical Aerosol Group (EPAG) impactor sub-team, Mark has also made recommendations to the Inhalanda working group, leading to subsequent revisions to Ph. Eur. and USP monographs.

SESSION 9: Testing protocols, stability issues and data requirements

Mr Jonathan Parks

SESSION ABSTRACT: An overview of the product quality, regulatory and safety aspects that must be considered when assembling an inhaled drug product application for regulatory submission. The components of the submission will be summarized with a more detailed look at the Manufacturing Product Control Strategy, QbD Approaches to product understanding and Product Stability studies as they relate to Inhaled Product Development and Industrialisation.

BIO: Jonathan has worked for 22 years at GSK’s Boronia site in Melbourne, Australia in the product development, quality assurance and technical functions. He has contributed to the development and successful worldwide registration of a number of new medicines in a variety of dose forms including sterile respiratory products for nebulisation using Blow-Fill-Seal technology as well as DPI respiratory products for a number of GSK’s principle respiratory medicines. He has an extensive background in the analytical aspects of the development of CMC packages for respiratory medicines including method development and validation, technology transfer, dose delivery characterisation and inhaled product and device testing. He is also a leader in application of lean and 6 sigma tools to laboratory operations and product capability analysis.
SESSION 10: Laser diffraction particle sizing and the practical applications and issues for measuring inhaler powders, sprays and finished product systems

Doctor - Ing. Ulrich Kesten

BIO: Dr. –Ing. Ulrich Kesten is the International Sales Director of Sympatec GmbH, a company in the field of Particle Size Analyser, established in 1984. He did a Master degree of Mechanical/Chemical Engineer at Technical University of Clausthal (TUC), Germany. After that, he started his work as scientific collaborator at the Powder Technology Institute of TUC and assistant of Prof. Dr. Kurt Leschonski until 1986. In 1986, he was promoted Dr.-Ing. He has authorised more than 30 publications in the field of Particle Technology, e.g. image analysis fibre optic sensors, isokinetic sampling, hydraulic slurry transport, particle size analysis. Dr.-Ing. Ulrich Kesten joined Sympatec GmbH as Sales Engineer in 1986. He is one of six shareholders of Sympatec GmbH and his responsibility is International Sales and Business Development.

SESSION 11: Keynote Address: “7 steps to successful pMDI” and Commercialisation of Regional Inhalation Products and Opportunities

Prof. Arvind Bhome /Prof. Hak Kim Chan

SESSION ABSTRACT: In this lecture the secrets of developing a successful pMDI will be reviewed. The science of pMDI formulating will be explained, as well as some of the technical pitfalls and their successful remedies. The full process from API selection to commercial launch will be reviewed, from formulation to device and analytical testing.
Professor Arvind Bhome

BIO: Pulmonologist Intensivist Professor for 3 decades. Involved in Transparent Single Dose DPI Concept in India in 1994-95. Convenor of Indian COPD Coalition. National Coordinator Asian network on Obstructive Lung Disease - a network of 12 Asian countries since 2008. Founder member & Ex- Vice President of Indian Society of Critical Care. Member International Council of Respiratory Care, AARC, USA.

Professor Hak Kim Chan

BIO: Hak-Kim Chan, Professor in Pharmaceutics, is leading the Respiratory Research Theme and the Advanced Drug Delivery Group at the Faculty of Pharmacy. He graduated from the University of Sydney (Ph.D. 1988 and D.Sc. 2009), was a postdoc at the University of Minnesota in 1988 – 1989 and a scientist at Genentech Inc in 1992 – 1995. While in Genentech, he was involved with the development of Pulmozyme (inhaled rhDNase for cystic fibrosis) and rhDNase powder aerosol formulation and delivery. Then he returned to Sydney where he played a pivotal role in the R&D of inhaled mannitol for bronchoprovocation and mucus clearance, leading to the Pharmaxis’ products Aridol and Bronchitol, respectively.

His research, funded primarily by the Australian Research Council and the pharmaceutical industry, focuses on inhalation drug delivery, ranging from powder production by novel processes, particle engineering and aerosol formulation to scintigraphic imaging of lung deposition and clinical outcomes. He has over 250 scientific publications on pharmaceutical formulation and drug delivery (with over 5000 citations and h-index 38) and holds seven patents in these areas. He is an executive editor of Advanced Drug Delivery Reviews and on the editorial advisory boards of various pharmaceutical journals including Pharmaceutical Research and International Journal of Pharmaceutics. He was appointed to the Subcommittee on Pharmaceutical Aerosol Standards for the Australian Therapeutic Goods Administration in 1996–97, and served as a member (2007 – 2008) on the in vitro – in vivo correlation subgroup of the International Pharmaceutical Aerosol Consortium on Regulation and Science in Washington DC. He is a Fellow of the American Association of Pharmaceutical Scientists (AAPS), Fellow of Royal Australian Chemical Institute (RACI), Chair of the NSW Pharmaceutical Science Group of the RACI, and Vice President of the Asian Federation for Pharmaceutical Sciences.
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Doctor Philip Kwok - For undertaking the role of head HKU host with steady determination. Bringing his local know how and bringing in a great crowd of keen participants to this event.

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And lastly to ALL of you our workshop participants whose openness and thirst for learning in this field has bought us together from across the globe. To exchange ideas, to open new doors, to solve mysteries and to lead you further into your own discoveries in this field.

Thank you

We hope you enjoyed it as much as we did!