CURRICULUM VITAE (ABBREVIATED)

Name: Hak-Kim Chan

Academic and Professional Qualifications: BPharm (NDMC, Taipei, 1983), PhD (Univ of Sydney 1988), Grad Cert Ed Studies (Univ of Sydney 1998), DSc (Univ of Sydney 2009)

Current Appointments:

2007 - Professor, Faculty of Pharmacy, University of Sydney
2009 - 2012 Visiting Research Professor, University of Hong Kong
2008 - 2010 Visiting Professor, National University of Singapore
2000 - 2010 Honorary Hospital Scientist, Royal Prince Alfred Hospital

Honours, Awards and Distinctions

2009 Excellence in Research Higher Degree Supervision Award, Faculty of Pharmacy, University of Sydney
2009 Japan Society for the Promotion of Science Fellow
2007 Disintiguished Lectureship, The Nagai Foundation Tokyo, for acheivement in pharmaceutical sciences
2006 Fellow of the American Association of Pharmaceutical Scientists
2005 Grand Prize of Innovation Challenge, University of Sydney
2004 Excellence in Teaching Award, Faculty of Pharmacy, University of Sydney
1999 John A Brodie Medal, the Institute of Engineers Australia
1989 Sigma Drug Delivery Prize 1989 Australia

Experience and Status

2002 - 2006 Associate Professor, Faculty of Pharmacy, University of Sydney.
2002 Acting Head of Pharmaceutics, Faculty of Pharmacy, University of Sydney.
1999 - 2001 Senior Lecturer, Faculty of Pharmacy, University of Sydney.
1995 - 1998 Lecturer, Department of Pharmacy, University of Sydney
1992 - 1995 Scientist, Department Pharm R & D, Genentech, Inc., USA.
1989 - 1991 Postdoctoral Fellow, Faculty of Pharmacy, University of Sydney.
1988 - 1989 Postdoctoral Associate, University of Minnesota, Minneapolis, USA.

Research performance

Over 250 scientific publications on pharmaceutical formulation and drug delivery (with a strong focus on inhalation aerosols), including 152 original research papers, 32 book chapters and reviews and over 100 conference articles, with over 1500 non-self citations. H-index 25.

Professional Appointments and Responsibilities

Vice President (2007 – 2011), Asian Federation for Pharmaceutical Sciences. The mission of the AFPS, which includes members from all countries in the Asia–Pacific, is to advance pharmaceutical sciences in the region, through research, education and a contribution to public policy.

Member (2008), Fellow Selection Committee, American Association of Pharmaceutical Scientists

Chair (2005–Present), the Royal Australian Chemical Institute (RACI) New South Wales Pharmaceutical Science Group. I was the first academic elected to this key position, which was traditionally filled by candidates from within the pharmaceutical industry. Focusing on bringing the

industry to academia, I have played a key role in organising local conferences for the pharmaceutical industry and giving seminars on career options for students.

Invited member (2006 – 2008) to serve on the *in vitro – in vivo* correlation subgroup of the International Pharmaceutical Aerosol Consortium on Regulation and Science in Washington DC.

Executive Committee Member (1995–2005), RACI NSW Pharmaceutical Science Group

Australian Therapeutic Goods Administration (TGA)

- *Appointed expert member* (1996 – 1997) to the Subcommittee on Pharmaceutical Aerosol Standards for the TGA. I contributed significantly to setting the testing standards required for the pharmaceutical inhalation products in Australia. Being in academia but previously having worked in the industry, I set requirements that are scientifically sound but also practicable for the industry to follow.
- *External assessor* (1998, 2005) on Inhalation products submitted to TGA for approval to market in Australia.

Editorial appointment: Executive Editor of Advanced Drug Delivery Review (impact factor 8.4)

Member of Editorial Advisory Boards: International Journal of Pharmaceutics, Pharmaceutical Research, Current Clinical Pharmacology, Recent Patents in Drug Delivery and Formulations, The Open Drug Delivery Journal, Recent Patents in Biotechnology, Pharmaceutical Technology Asia, Journal of Drug Delivery Science & Technology, Journal of Biomedicine and Biotechnology.

Conference and symposium chairs of key scientific events

- Particulate Processes in the Pharmaceutical Industry III, 2011 (Co-Chair)
- Fluid/particle systems in Pharmaceutical Industry (Session Co-Chair), 5th World Congress on Particle Technology 2006.
- Royal Australian Chemical Institute Pharmaceutical Science Group Inaugural Research Student Symposium 2005.
- Symposium on Nanoparticles for Therapeutic Applications, 7th World Biomaterials Congress 2004.
- Australian Aerosol Symposium (an international aerosol symposium jointly sponsored by the International Society for Aerosols in Medicine, ANZSRS, and TSANZ), 2001.

Conference organising committees

- 2nd AFPS Conference, Kyushu, Japan 2009.
- 17th International Symposium on Microencapsulation in Nagoya, Japan 2009.
- Pan Pacific International Conference on Pharmaceutical and Life Sciences, Nagoya, Japan 2008.
- The 7th International Conference on the Electrical, Transport and Optical Properties of Inhomogenous Media, Sydney 2006 (responsible for the bio-composite session).
- 15th International Congress of International Society for Aerosols in Medicine (ISAM), Perth 2005 (responsible for the entire pharmaceutical industry program).
- International Workshop on High Gravity Technology and Related Process Intensification Engineering, Beijing 2005 (mainly contributed to the pharmaceutical session).

Invited speaker in major national conferences and international conferences held locally in Australia

- AUS Chapter Controlled Release Society Conference (2009)
- Bioaerosol Workshop (Sydney 06) – Lung deposition of bioaerosols.
- Australiasian Pharmaceutical Science Association Annual Scientific Conference (Melbourne 95&96) – Pharmaceutical aerosol formulations.
- International Society for Aerosols in Medicine (Perth 05) – Research of aerosols in medicine in Australia.
- Australian and New Zealand Society of Respiratory Science (Perth 95) – Advances in respiratory drug delivery.

- World Biomaterials Congress 7 (Sydney 04) – Biocomposite particles for inhalation.
- World Congress on Particle Technology 4 (Sydney 02) – Pharmaceutical inhalation aerosol delivery.
- Thoracic Society of Australia and New Zealand (Brisbane 01) – Advances in novel inhaler devices.

Invited speaker in major international conferences overseas

- 1000 Years of Pharmaceutical Aerosols – What Remains to be Done, A Forward Looking Meeting Combination Therapies (Reykjavik 2009) – Combination inhalation products.
- 2nd Asian Federation for Pharmaceutical Sciences Conference (Kyushu 2009) – The story of Aridol™, inhaled mannitol for diagnosis of asthma.
- 1ST International Symposium for Industrial Pharmacy & Clinical Pharmacy (Guangzhou, 2009) – The development of mannitol for inhalation as a successful commercial product.
- PharmSci@Asia Symposium (Nanjing, 2009) – Pulmonary drug delivery using dry powder aerosols.
- Royal Golden Jubilee International Congress IX (Pattaya 08) – deposition of dry powder aerosols in the lungs.
- Pan Pacific International Conference on Pharmaceutical and Life Sciences (Nagoya 08) – Dry powder inhalation aerosol delivery to the lungs.
- Asian Association of Schools of Pharmacy (Philippines 07) – From powder production to lung deposition of inhaled aerosols.
- Respiratory Drug Delivery - Europe (Paris 07) – Role of particle morphology in powder inhalers.
- *15th* Nisshin Particle Technology International Seminar (Awajishima 06) – Pharmaceutical inhalation aerosols.
- International Workshop on High Gravity Technology & Process Intensification Engineering (Beijing 05) – Nanoparticles and pharmaceutical aerosol applications.
- International Conference on Organized Molecular Films (LB 11) (Hokkaido 05) – Opportunities for colloid scientists in pulmonary drug delivery.
- International Symposium on Nanomaterials Technologies and Applications (Beijing 01) – Inhalation drug delivery of fine particles.
- International Society for Aerosols in Medicine (Vienna 99) – Novel imaging techniques to measure *in vivo* aerosol deposition in the lungs.
- American Institute of Chemical Engineers (Denver 94) – Crystal engineering to produce different shaped particles with aerodynamic advantages.
- American Association of Pharmaceutical Scientists (San Antonio 92) – Delivery of therapeutic proteins, rhDNase

Assessor of grant proposals

Australian Research Council; National Health & Medical Research Council; Asthma Foundation of New South Wales; Australian Cystic Fibrosis Research Trust; Medical Research Fund of Western Australia; Biomedical Research Council Singapore, Science Foundation Ireland, Medical Research Council – United Kingdom.

External Assessor for academic promotion

2005 Promotion to Associate Professor, College of Pharmacy, Virginia Commonwealth University
2004 Promotion to Associate Professor, School of Pharmacy, Washington State University

Consultant to the pharmaceutical industry

Consultant to the pharmaceutical industry over the last 10 years including Fisons Pharmaceuticals, Aradigm Corporation, AMRAD Corporation, Allersearch, Bayer, Faulding, Rhone-Poulenc Rorer Aust Pty Ltd, Progen Industries Ltd, Pfizer, Peptech, Epitan, 3M Pharmaceuticals, Novartis,

Vapotronics, Novogen, Aventis, Ferring, Eiffel Technologies, Canon, Pharmaxis, MAP, NanoMaterials Technology.
Expert witness for patent attorneys on patent opposition cases – Philips Ormonde & Fitzpatrick Aust & NZ patent attorneys 2005; Goldman Partners 2004; Clayton Utz 2003.

Media contributions
Contributions to the following media on powder aerosol inhalers: Current Therapeutics 5/2000, Northern Downs News 4/2000, Australian Pharmacy Trade 4/2000, Sunshine TV, Medical Observer, & Aust J Pharmacy 8/2000.

Research Training
Supervised 13 PhDs, 3 MSc and 8 postdocs along with over 40 Honours students and international visiting research students; currently supervising 3 PhD students.

Creative Achievements in the Application of New and Existing Science and Technology

Note: the references in [ ] correspond to those in the list of 10 key publications.

Inhalation aerosol delivery of therapeutic proteins. While working in Genentech Inc, USA I was involved in major breakthrough of aerosol delivery of therapeutic proteins using recombinant human deoxyribonucelase (rhDNase, Pulmozyme®) for the treatment of cystic fibrosis. Pulmozyme® is the only protein product marketed for delivery to the lungs by aerosols. I identified the excipients that can stabilise rhDNase in powder formulations and has successfully developed and patented drug powder aerosols for the protein [patents (i) & (ii) below].

Mannitol aerosols for more precise asthma diagnosis. I played a pivotal role in the development of dry powder mannitol aerosols for the diagnosis and delivery of drugs for asthma, and the delivery of drugs for impaired mucociliary clearance in diseases such as cystic fibrosis, bronchiectasis and chronic bronchitis [5,7]. The product (Aridol™, Pharmaxis Ltd) for asthma diagnosis has recently been approved for sale in Australia and 14 countries across Europe, including the UK, Germany, France, Italy, Sweden, Denmark, Ireland, and the Netherlands. Working with the Australian lung physiologist, Dr Sandra Anderson, I developed the first successful bench-to-market inhalation aerosol product, wholly within Australia. The inhaled mannitol aerosol provides an important disease management tool to millions of asthma sufferers, and is particularly valuable as an objective assessment test for the early detection of asthma in young children.

Novel methods for the production of fine powders for aerosol delivery. Supported by the ARC-Linkage and NHMRC Development grants, I have collaborated closely with the pharmaceutical industry, including Canon, Vapotronics, Pharmaxis, Nanomaterials Technology and 3M Pharmaceuticals, which has lead to two patents in novel processes of producing particles [patents (iii) – (v) below].

Innovative imaging services. Supported by a grand prize of the Innovation Challenge of the University of Sydney 2005, we set up an operation PharmaScint under the Woolcok Institute to provide medical imaging services – clinical imaging trial, data management, and analysis solutions – to the pharmaceutical industry in Australia and world-wide. The focus on this niche market is to aid clients in evaluating optimal delivery routes and efficacy for new pharmaceuticals (current global drug delivery market >US$50 billion). The business involves the use of gamma-scintigraphic imaging as a therapeutics developmental tool. PharmaScint focuses on the largely untapped market of three dimensional (3D) imaging studies of drug delivery and bio-distribution using single photon emission computed tomography (SPECT) and positron emission tomography (PET). PharmaScint is headed by myself, A/Prof Dale Bailey (Nuclear Physicist, Royal North Shore Hospital, RNSH) and Dr Paul Roach (Head of Department of Nuclear Medicine, RNSH).

I hold six key patents on aerosol formulations and delivery. The two patents in 1995 describe protein formulations developed whilst working in Genentech, Inc. I filed the other four over the last five years whilst at the University of Sydney. Of particular note is patent no. 3, which was jointly held by the University of Sydney and UNSW, and was a result of research funded by the ARC. These achievements show strong evidence of my leadership and entrepreneurial skills in commercialisation of research: *(i) WO 9523613 Pharmaceutical Acceptable DNase Inhalant, 1995; (ii) WO 9523854 Improved DNase Liquid Solutions Using Calcium and Sugars to Enhance Storage, 1995; (iii) WO 0245690 Synthesis of Small Particles of Biologically Active Agents, such as pH-sensitive Proteins; (iv) WO 0294342 European Patent EP 1 389 137 B Compositions for Protein Delivery via the Pulmonary Route; (v) WO 0696906 Inhalable drug; (vi) PCT/AU/2008/000630 'Composite carriers for dry powder inhalation therapy'.*

Achievements in Advancing Fundamental Science in the Field.

Physical parameters influencing dry powder aerosol performance. My work has led to a major advance in defining the key factors that affect the dispersion of powders to form aerosols, including the relationship between particle size, air flow and inhaler-device efficiency [8]. Such information has been difficult to obtain in the industry because the particle size and/or the inhaler is usually fixed early in the R&D phase. It was also difficult in the university research context because a well-defined model powder system was not available. Through the technique of spray drying and applying my industry experience, I solved the problem by using chemically and morphologically well-defined particles of mannitol which differ only in their size.

Particle engineering for aerosol delivery. I first developed particle engineering techniques to produce elongated particles with improved aerodynamic behaviour of anti-asthmatic aerosol powders [10]. This work was awarded the *Sigma Drug Delivery Prize* in 1989. I have since reconceived those methods in producing corrugated particles for the same purpose, by substituting conventional crystallisation with precisely controlled techniques of spray drying. This resulted in opportunities for further improving the aerodynamic behaviour of other major drugs, in particular, protein-based compounds. I announced this innovation in a plenary lecture on the role of particle morphology in powder inhalers at the presitigious *Respiratory Drug Delivery Conference* in April 2007 in Paris.

Inhalers. Computational fluid dynamics (CFD) has been widely used by industry engineers in the modelling of fluid systems. My group uniquely applied CFD in developing a deep understanding of inhaler design and performance—previously understood only in rudimentary terms of air tuburlence and particle collisions. We generated new information about air flow patterns inside an inhaler, data that were previously difficult to obtain experimentally [2]. We accurately delineated and expanded the role of a grid as an air flow rectifier, which was previously described simply as a retainer of capsule fragments. To enhance the inhaler performance, we found that increasing turbulence by reducing the inhaler air-inlet dimension must coincide with the release of powder into the air stream. These concepts, developed over the past five years, have produced significant interest from the major pharmaceutical companies in the field, including Pfizer and GSK and has benefited the Australian company Pharmaxis via two current ARC-LPs.

Characterisation of the electrostatic properties of inhalation aerosols. My group was the first to establish the use of an electrical low-pressure impactor (ELPI) for the simultaneous measurement of both the charge and aerodynamic size distributions of aerosol particles [1]. This technique is far superior to the conventional Faraday pail, which is limited to measuring only net charge measurement rather than the charge distribution in particle-size fractions. Using an ELPI, we revealed significant disparities between the charge profiles of commercial metered dose inhalers (MDIs). These findings have practical ramifications for the lung deposition of MDI aerosols, with potential benefits to the community through improved health outcomes and the more closely

targeted regulation of generic aerosol products. Our MDI paper [1] was quoted in the US publication *Pharmacy Choice* [http://www.pharmacychoice.com/News/article.cfm?Article_ID= 21392] and guides correct professional decision-making. Our findings are currently implemented by a number of research teams, including other world leaders in the field, Profs AJ Hickey in North Carolina and PR Byron in Virginia, U.S.A [Int J Pharm 2007; 336:352-360; J Aerosol Med 2009; 22:1-11].

In-vivo characterisation of aerosol deposition in the lungs. I collaborated with the Australian nuclear physicist, Prof S Eberl, to develop his single-photon emission computed tomography (SPECT) into a rapid, dynamic technique to investigate the 3D distribution of aerosol inhaled to the lungs [4]. Our one-minute protocol eliminates the problem of aerosol clearance encountered in conventional SPECT, which previously required up to 30 minutes of imaging (thus delivering images of low accuracy). It has provided the first clear evidence of the differences in lung deposition from the hygroscopic growth of aerosols during transit in the airways. I presented an invited plenary lecture on this work at the *International Society of Aerosol in Medicine* Conference 1999 and, again in 2005, with new applications employing dry powder aerosols. The rapid technique and the high-resolution 3D images that it produces have streamlined research design in aerosol drug testing. Applying this innovative technique in a recent study, I have provided evidence on the precise effect of particle size on the lung deposition of polydisperse dry powder aerosols. Our imaging work on lung deposition and clearance is world-leading and has been cited 169 times in total.

A list of 10 key publications

1. Kwok PCL, Glover W and **Chan H-K** (2005) Electrostatic charge characteristics of aerosols produced from metered dose inhalers. *Journal of Pharmaceutical Sciences* 94(12): 2789-99.
   First study to provide information on the electrostatic charge in aerosols of commercial metered-dose inhalers ('puffers') for asthma.
2. Coates M, Fletcher D, **Chan H-K** and Raper J (2004) Effect of design on the performance of a dry powder inhaler using computational fluid dynamics. Part 1: Grid structure and mouthpiece length. *Journal of Pharmaceutical Sciences* 93: 2863-2876.
   First study using computational fluid dynamics to provide a mechanistic understanding for the design of inhaler devices.
3. **Chan H-K** (2003) Formulation challenges: protein powders for inhalation. In *Modified-Release Drug Delivery Systems*, Rathbone MJ, Hadgraft J, Roberts MS (Ed), Marcel Dekker, New York, pp. 879-890 (invited).
   Provided feasible solutions to enhance the stability of protein aerosol powder formulations
4. Eberl S, **Chan H-K**, Daviskas E, Constable C and Young I (2001) Aerosol deposition and clearance measurement: a novel technique using dynamic SPET. *European Journal of Nuclear Medicine* 28: 1365-1372.
   The world fastest techniques which take only one-minute instead of 30-minutes by conventional methods to accuratly image aerosol deposition in the lungs
5. Leuppi JD, Salome CM, Jenkins CR, Anderson SD, Xuan W, Marks GB, Koskela H, Brannan JD, Freed R, Andersson M, **Chan H-K** and Woolcock AJ (2001) Predictive markers of asthma exacerbation during stepwise dose-reduction of inhaled corticosteroids. *American Journal of Respiratory Critical Care Medicine* 163: 406-412.
   Successful application of mannitol powder aerosols developed in my laboratory to monitor asthma treatment by inhaled steroid drugs
6. Bustami R, **Chan H-K**, Dehghani F and Foster NR (2000) Generation of micro-particles of proteins for aerosol delivery using high pressure modified carbon dioxide. *Pharmaceutical Research* 17: 1360-1366.

Pioneer work on using supercritical fluid to produce respirable particles of therapeutic proteins from their aqueous solution.

7. Robinson M, Daviskas E, Eberl S, Baker J, **Chan H-K**, Anderson SD and Bye PTP (1999) The effect of inhaled mannitol on bronchial mucus clearance in cystic fibrosis patients: A pilot study. *European Respiratory Journal* 14: 678-685.
   Successful application of mannitol powder aerosols developed in my laboratory to enhance clearance of mucus from the lungs of CF pateints
8. Chew N and **Chan H-K** (1999) Influence of particle size, air flow and inhaler on the dispersion of mannitol powders as aerosols. *Pharmaceutical Research* 16: 1098-1103.
   First fundamental study to establish a clear relationship between particle size of drug powders, inhaler efficiency and air flow rate.
9. **Chan H-K**, Clark AR, Gonda I, Mumenthaler M and Hsu C. (1997) Spray dried powders and powder blends of recombinant human deoxyribonuclease (rhDNase) for aerosol delivery, Pharmaceutical Research 14: 431-437
   First study to show the feasibility of producing chemically and physically stable powders of therapeutic proteins by spray drying for inhalation drug delivery
10. **Chan H-K** and Gonda I (1989) Aerodynamic properties of a solid form of cromoglycic acid. *Journal of Aerosol Science* 20: 157-168.
    First study using particle engineering to produce elongated particles of an anti-asthmatic drug with aerodynamic advantages

A full list of publications is attached separately.