



SAPA-GP Members Conference Series 2009-2010

Biologics Drug Development Conference

Saturday, March 6, 2010

**Holiday Inn Philadelphia North
Fort Washington Hotel & Conference Center**

432 Pennsylvania Avenue, Fort Washington, PA 19034
(215) 643-3000

Organizing Co-Chairs:

Peter Luo, Ph.D.

Laura Hong, Ph.D., Senior Research Scientist in MRL, Merck

Zhibiao Fu, Ph.D., Principal Scientist, Biopharma R&D, GSK

The SAPA-GP Biologics Drug Development Conference is a follow up event for the 2008-2009 annual conference biologics session. It is designed to encompass the introduction of the general principles of all spectrum of the biologics drug development, and to provide attendees with an overview of the challenges and opportunities and the possibility of entering to the \$34 Billion Industry. Expert speakers from the major players in biologics industry will discuss opportunities and challenges in the biologics with the emphasis on the following parts:

- Monoclonal antibodies discovery, which covers > 30% of the biologics
- DMPK and safety study of the biologics during the early discovery stage
- Bioprocess development and the manufacturing of biologics
- Bioanalytical and formulation of the biologics
- Regulatory requirement of the biologics
- Current biologics development status in China

Sponsors:



Agenda

8:30-9:00 Registration

Morning Session

Monoclonal antibodies discovery, DMPK and safety

This session will discuss the target identification, monoclonal antibodies generation and screening. It will also include the DMPK and safety study of the biologics.

Moderator: Peter Luo, Ph.D.

9:00-9:05 Welcome and Introduction
Tsang-Bin Tzeng, Ph.D., President; SAPA-GP

9:05-9:10 Opening Remark and Program Overview
Peter Luo, Ph.D.

Keynote Presentation

9:10-9:50 **Current challenges and opportunities for Biologics drug discovery and development**

Herren Wu, Ph.D.

VP, Global Head of Technology and Lead Generation,
Head of Antibody Discovery & Protein Engineering, MedImmune

9:50-10:20 **Pre-clinical Safety Assessment of Biopharmaceuticals**

Danuta Herzyk, Ph.D.

Senior Scientific Director, Merck

10:20-10:50 **Pharmacokinetics/pharmacodynamics (PK/PD) of therapeutic proteins: what can we leverage from what we have learnt from small molecules?**

Honghui Zhou, Ph.D.

Senior Director and Head Pharmacokinetics,
Modeling & Simulation, Biologics Clinical Pharmacology,
J&J Centocor R&D

10:50-11:00 *Coffee Break & Networking*

11:00-11:30 **Current trends to antibody generation and engineering**

Peter Luo, Ph.D.

11:30- 12:00 **Best Practice Guidelines for the Validation of Immunoassays Assays for Pharmacokinetic Studies of Macromolecules**

Russell Weiner, Ph.D.

Group Director, Bioanalytical Science,
Pharmaceutical Research Institute, BMS

12:00-1:00 *Lunch (free for registered attendees) and Networking*

Afternoon Session

Bioprocess development, manufacturing, formulation and regulatory

This session will discuss the biologics process development and manufacturing according to the regulatory requirements.

Moderator: Laura Hong, Ph.D., Merck; Zhibiao Fu, Ph.D., GSK

Keynote Presentation

1:00-1:40 **Challenges for the biologics manufacturing**

Bruce Vickroy, Ph.D.

Senior Technology Manager, BioPharm Global Manufacturing and Supply,
GSK

1:40-2:10 **Cell culture process for antibody production**

Zhong Liu, Ph.D.

Director of Biotechnology Development, Shering-Ploung/Merck

2:10- 2:40 **Microbial hosts and expression systems for the biologics**

Sandro Nalli, Ph.D.

Principal Scientist, Biopharma R& D, GSK

2:40- 3:00 *Coffee Break & Networking*

3:00-3:30 **Downstream process development for large-scale production of therapeutic antibodies: challenges and opportunities**

Dave Jen, Ph.D.

Head of Purification Process Development Technical Operations, Alexion
Pharmaceuticals

3:30- 4:00 **Analytical Characterization of Antibody Therapeutics from Regulatory Filing Perspectives**

Mingfang Hong, Ph.D.

Principal Research Scientist, J&J Centocor R&D

4:00-4:30 **Overcoming the Physical Barriers for Delivery of Large Molecules**

Henryk March

Senior Investigator, Bioprocess and Bioanalytical Development, Merck

- 4:30-5:00 **Regulatory Considerations when Developing Biologics**
Melissa Tice, Ph.D.
Director in the Worldwide Regulatory Affairs Group, Merck Research
Laboratories
- 5:00-5:20 **General considerations for Developing and Validating Cell-Based
assays**
Uma Prabhakar, Ph.D.
Vice President, Biomarker Research & Biological Services
Frontage Laboratories
- 5:20-5:40 ***Biologics CRO in China and US***
Larry Wang, Ph.D.
President at GenScript Corporation
- 5:40 **Concluding remarks and *adjourn***

Speakers' Bio's

Listed alphabetically based on the last name

Danuta Herzyk Hrebien, Ph.D.

Senior Scientific Director, Global Compound & Program Management Safety Assessment, Merck Research Laboratories

Abstract

Pre-clinical Safety Assessment of Biopharmaceuticals

Safety assessment studies with biotechnology drug candidates require program-tailored approaches and are driven by target biology and clinical study design. Thus, good understanding of both the target biology and the structural attributes of a biologic drug candidate are essential in species selection for toxicology studies. In addition, in-depth characterization of pharmacodynamic and pharmacokinetic (PK/PD) profiles in toxicology species greatly contributes to safety assessment of biotechnology products. In addition, potential immunogenicity (anti-drug antibody response) in animals to these products presents a unique challenge and has to appropriately addressed in the context of toxicity data interpretation.

Biography

Dr. Danuta Herzyk (native of Poland) earned her MS degree in Pharmaceutical Sciences and Ph.D. in Clinical Immunology and Biochemistry from the Medical University of Wroclaw (*pronounced: Vrotzlav*), Poland.

In 1985 Dr. Herzyk accepted a postdoctoral position at the Ohio State University in Columbus, OH and moved to USA. Her postdoctoral research was conducted with Dr. Richard Mortensen in the Department of Microbiology and Immunology and with Dr. Mark Wewers in the Department of Pulmonary and Critical Care Medicine. Her research areas included the role of IL-1 in regulation of acute phase responses, and oxidative intermediates and cytokines, mainly IL-1 β and TNF α , in pulmonary diseases.

Dr. Herzyk joined the Department of Safety Assessment at GlaxoSmithKline R&D in 1992 and overtime became a Director of Immunologic Toxicology. Her work involved mainly the development of biopharmaceuticals. In 2007, Dr. Herzyk took a position of Senior Scientific Director in the Department of Safety Assessment at Merck & Co. Currently she is overseeing the preclinical development of biopharmaceuticals and vaccines.

Dr. Herzyk is a member of the Society of Toxicology, including Immunotoxicology Specialty Section, the Drug Information Association and the ILSI/HESI Immunotoxicology Technical Committee. She has published over 40 articles and book chapters in immunology and toxicology fields, edited a handbook for immunotoxicologists, and serves as member of the Editorial Board of journal entitled *Perspectives in Experimental and Clinical Immunotoxicology*.

Mingfang Hong, PhD

Principal Research Scientist, J&J Centocor R&D

Dr. Mingfang Hong is currently a Principal Research Scientist within Large Molecules Method Development department of J&J Centocor R&D, located at Radnor, PA. His major responsibilities include analytical methods development and validation, protein molecules characterization, process development support, and QC lab support. Dr. Hong has 9+ years' biopharmaceutical industry experiences.

Prior to joining J&J Centocor, Dr. Hong had worked for Bristol-Myers Squibb for 2 years. He obtained his Ph. D. degree in Analytical Chemistry from Indiana University at Bloomington and his BS degree in Chemistry from Peking University.

Dave Jen, Ph.D.

Head of Purification Process Development Technical Operations, Alexion Pharmaceuticals

Prior to joining Alexion Pharmaceuticals in October 2008, Dr. David Jen spent 10 years in Centocor R&D, a division of Johnson & Johnson and led the establishment and operation of cGMP and Technology Development Pilot Plants in areas of cell culture and purification development and manufacturing with facilities totaling more than \$40MM. Prior to Centocor, he spent 6 years in several biotech companies in California with responsibilities in early and late phase manufacturing support and process development for biopharmaceutical products, including bacteria plasmid DNA, recombinant proteins and stem cell. Dr. David Jen is currently head of Purification Process Development for monoclonal antibodies and recombinant proteins in Alexion Pharmaceuticals, supporting 10,000L bioreactor commercial production process in Rhode Island and new product development in Connecticut.

Contributing to the licensure of two monoclonal antibodies and the development and production of numerous antibodies targeting oncology, hematology and immunology diseases, Dr. David Jen's experience spans upstream (fed batch and perfusion cell culture), downstream purification, formulation as well as process engineering and CMC. Dr. David Jen's is a frequent invited speaker for downstream purification and Quality by Design in national conferences and professional societies. He has been leading QbD effort aiming to improve process understanding and process efficiency to allow continuous improvement in a life cycle approach to meet visions of FDA's 21st Century cGMP initiatives. Dr. David Jen obtained his Ph.D. in Chemical Engineering from University of Cincinnati and B.S. in Chemical Engineering in National Cheng Kung University

Zhong Liu, Ph.D.

Director of Biotechnology Development, Shering-Ploung/Merck

Dr. Zhong Liu is a director of Biological & Sterile Product Development (Union, NJ) in Biologics Research of Merck Research Laboratories. He joined Schering-Plough Research Institute (Merck) in 1998 and currently leads the Protein Expression Technologies group responsible for the generation of production cell lines for biologics. Dr. Liu received his Ph.D. in Cell Biology from the University of Connecticut Health Center in 1994. After a brief post-doctoral training at the Fred Hutchinson Cancer Research Center (Seattle, WA), he began his industrial career as a scientist at Berlex Bioscience (Schering AG, Richmond, CA) in 1994.

Dr. Liu received his pre-med training at Beijing University (1981-1984) and received his medical training at Peking Union Medical College (1984-1988).

Peter P. Luo, Ph.D.

Dr. Peter Luo is an expert in protein folding, engineering and antibody phage library technology. From May 2006 to Feb 2010, he served as the Director of Biologics at Merck & Co., Inc. and Chief Technology Officer of Abmaxis Inc. Peter headed the Abmaxis group in building in house phage antibody libraries and its application to novel biologics. Prior to founding Abmaxis, Peter was the first lead scientist in Xencor that was cofounded by Dr Steve Mayo at Caltech and established its protein chemistry department. Peter has computationally designed and experimentally confirmed the first stabilized variants of GCSF with in vitro and in vivo efficacies. This designer protein was featured in Forbes "Better than Mother Nature", *an article on Biotech, Forbes, January 25, 1999*. Peter has extensive experience in designing and studying the folding, stability and activity of peptides, proteins, and DNA by applying a broad multi-disciplinary approach that combines methods and ideas of experimental and computational biology, chemistry and physics.

Peter received a postdoctoral fellowship from the Arthritis Foundation in studying protein folding & design with Dr. Robert Baldwin at Stanford University. He received his Ph.D. with Dr David Lynn in physical and bioorganic chemistry from The University of Chicago, a MS degree in applied physics from The Institute of High Energy Physics of the Chinese Academy of Sciences, and a B.S. degree in chemistry from Peking University.

Henryk March

Senior Investigator, Bioprocess and Bioanalytical Development, Merck

Henryk joined Merck's newly created protein formulation group in 1990, working under direction of Russ Middaugh. Since then he continued to focus on biophysical properties of biologics and vaccines, developing a number of novel methodologies related to spectroscopic properties (e.g. UV second derivative multicomponent analysis) and production processes (e.g. dis/reassembly of Papillomavirus virus-like particles). He published 8 book chapters and over 30 papers. He holds Master Degree in Biotechnology from University of Krakow, Poland.

Sandro Nalli, Ph.D.

Principal Scientist, Biopharma R& D, GSK

Sandro Nalli attained his PhD in Chemical Engineering in 2005 at McGill University, Montreal, Canada. His graduate work focused on the biochemistry and modeling of microbial interactions with industrial pollutants. Once completed, he started a research associate position at the Structural Genomics Consortium (SGC) in the University of Toronto, Canada. At the SGC his time was split between functions including: Bioreactor/Biosensor Design and Development; Protein pipeline management; Involvement in a Biotech spin-off (Harbinger Biotechnology and Engineering); Protein expression experimentation and high-throughput protein production screening. In 2006 he held the position of Development Scientist at Sanofi-Pasteur, working on automation and technology implementation in the department of Process Development, Fermentation. In 2008 Sandro obtained his current position of Principal Scientist at GlaxoSmithKline, where he is responsible for fed-batch fermentation process development and screening with *Saccharomyces cerevisiae*, *Pichia pastoris* and *Escherichia coli* recombinant systems in the Microbial and Cell Culture department of Biopharmaceutical Process Development. He is now completing an MBA at Lehigh University focusing on Finance.

Uma Prabhakar, Ph.D.

Vice President, Biomarker Research & Biological Services Frontage Laboratories

Dr. Uma Prabhakar is currently a Vice President of Biomarker Research & Biological Services at Frontage Laboratories, a CRO based in Malvern, PA. Prior to that, as a Senior Director in the Department of Clinical Pharmacology & Experimental Medicine, she was responsible for the management, assessment and reporting of the characterization of the pharmacodynamics, immune function and immune response of Centocor and J&J's Oncology and IMiD drugs (antibody therapeutics) across preclinical GLP studies and Clinical Phase I-IV trials. Subsequently, she was responsible for the management of the translational and biomarker research related activities for Centocor and J&J's Oncology. Dr Prabhakar worked for Glaxo SmithKilne from 1986-2001 in both Discovery Research and Clinical Pharmacology in various roles of increasing responsibility and was responsible for identifying, initiating and leading various research projects (small drug molecules) and also in the development and validation of pharmacodynamic marker

assays to be used in the evaluation of compounds in early and late-phase clinical studies in the therapeutic areas of inflammation and bone metabolism. She has broad experience with *in vivo* and *in vitro* pharmacology in the following therapeutic areas: rheumatology, oncology and bone and extensive knowledge and experience in preclinical and clinical aspects of Oncology and Translational Medicine & Biomarkers.

Dr. Prabhakar has a strong cell-based assay development background and has made contributions to the immunogenicity characterization of brand-name drugs such as Remicade™, Simponi™, Stelara™. She has also contributed to the preclinical aspects of the anti-asthma drug, Airiflo™. She has published a book, 'Validation of Cell-Based Assays in the GLP Setting, published by John Wiley in 2008. Dr. Prabhakar obtained her Ph.D degree in Human Genetics in 1980 from Osmania University, Hyderabad, India.

Melissa Tice, Ph.D.

Director in the Worldwide Regulatory Affairs Group, Merck Research Laboratories

Dr. Tice is a Director in the Worldwide Regulatory Affairs Group (WRG) in Merck Research Laboratories and associated with the development of biological oncology products. Her role is to address, guide and strategize the team in regards to the regulatory aspects of the global development of the product from early to late clinical stages and to coordinate all regulatory agency interactions. Prior to joining Merck, Dr. Tice led the Gene Therapy and Biotechnology Group in Worldwide Regulatory Affairs at Schering-Plough Research Institute. Prior to regulatory affairs, Dr. Tice was a Senior Principal Scientist in CNS/CV Pharmacology Department at Schering-Plough Research Institute. Dr. Tice received her undergraduate degree in Chemistry from Douglass College, Rutgers University in New Brunswick, NJ, a doctorate in Biological Chemistry from the University of Pennsylvania in Philadelphia, PA. and postdoctoral training at the centers of NINCDS and NIAAA at the National Institutes of Health in Bethesda, MD.

Bruce Vickroy, PhD.

Sr. Technology Manager, BioPharm Global Manufacturing and Supply, GlaxoSmithKline

Bruce Vickroy is currently a production process technology expert within GSK's manufacturing division Global Manufacturing and Supply (GMS) <http://www.gsk.com/collaborations/biopharm-manufacturing.htm>. Bruce manages the transfer of the process technology from GSK R&D or external clients and provides technical support for ongoing manufacturing activities. Bruce has contributed to process scale-up, equipment design, process troubleshooting and process data analysis.

Prior to joining the manufacturing division in 2004, Bruce worked in GSK R&D for 18 years developing numerous biological based processes and transferring these processes to manufacturing facilities and organizations. Bruce developed mammalian and insect cell culture processes and some microbial processes including initial harvest step development. The range of products included antibiotics, antibodies and recombinant proteins. Bruce worked on a variety of cell culture and microbial technologies in

development or manufacturing ranging from adherent cell culture to continuous membrane recycle microbial systems.

Bruce received a BS in chemical engineering from the University of Delaware and a PhD also in chemical engineering from the University of California at Berkeley.

Larry Wang, PhD
President, GenScript Corporation

Dr. Larry Wang is the co-founder and President of GenScript, a biology CRO company based in New Jersey, USA with manufacturing sites at Nanjing, China. The CRO service of GenScript is focused on early drug discovery. GenScript provides services ranging from molecular biology, protein expression, peptide synthesis, antibody production, to assay development.

Prior to GenScript, Dr. Larry Wang worked as a Senior Principal Scientist at Bioinformatics Group of Schering-Plough from 1996 to 2002. He is one of the key inventors on the target discovery work for Zetia, which advances the understanding of intestinal cholesterol pathway. His scientific achievement has been recognized with a presidential award by Schering-Plough, and Gallo Award from Cancer Research Institute of New Jersey.

Prior to Schering-Plough, Dr. Larry Wang got his Ph. D. from Rutgers University in 1996, and his BS degree in Biochemistry from Shandong University, China in 1991. Dr. Larry Wang has over 20 publications in leading scientific journals.

Russell Weiner, PhD
Group Director, Biomarker and Bioanalytical Sciences, Bristol-Myers Squibb Research & Development

Abstract

Best Practice Guidelines for the Validation of Immunoassays Assays for Pharmacokinetic Studies of Macromolecules

Immunochemistry based assays are the method of choice for quantifying macromolecule therapeutics in pharmacokinetic samples derived from non-clinical and clinical studies. However, there currently does not exist harmonized bioanalytical methods validation regulatory guidance specifically aimed at this class of assays. To best facilitate the creation of such guidance, based on strong scientific principles, a diverse committee comprised of individuals from Pharma, Biotech, and CRO organizations have developed a best practices document. This document specifically describes a standardized approach for method development, pre-study and in-study validation of quantitative immunoassays for macromolecules. Recommendations arising from this consensus based approach have now been used successfully for several years and should have the best opportunity of

being considered by regulatory agencies in their development of appropriate guidance. This presentation will address the critical assay parameters which should be evaluated.

Biography

Russ Weiner is currently Group Director of Biomarker and Bioanalytical Sciences at Bristol-Myers Squibb. In this role he is responsible for discovery and regulated bioanalysis in support of PK, immunogenicity and biomarker assay development, validation and sample analysis. Russ received his Ph.D. in Biochemistry from Albany Medical College and in 1993 joined the BMS. During his tenure at BMS, Russ directed the Clinical Biomarker Development group combining the technologies of immunochemistry, LC/MS, molecular biology, molecular pathology and flow cytometry. Russ broadened his non-bioanalytical responsibilities to include Chairing the Immunology-Early Development Team. In this role Russ served as study director on over a dozen Phase I/II clinical studies, transitioning 8 compounds from discovery to IND.

Russ is an active member of Applied Pharmaceutical Analysis (APA) and the American Association of Pharmaceutical Scientists (AAPS). He currently serves as the co-Chair of the 2010 APA meeting and has served as the Chair of the AAPS 2009 Annual Meeting and Chair of the Biotechnology Section. Russ has co-chaired and/or participated in several AAPS workshops that focused on translational medicine, biomarkers and regulated bioanalysis. His participation resulted in co-authorship of several workshop reports on bioanalytical method validation (large and small molecules), incurred sample reanalysis and biomarker analysis. In addition, to his workshop involvement, Russ has co-authored two white papers including “Recommendations for the Bioanalytical Method Validation of Ligand-Binding Assays to Support Pharmacokinetic Assessments of Macromolecules” and “Fit-for-Purpose Method Development and Validation for Successful Biomarker Measurement”.

Herren Wu, PhD

Vice President, Global Head of Technology and Lead Generation, Medimmune

Dr. Herren Wu is vice president of R&D, global head of technology and lead generation, and head of antibody discovery and protein engineering in MedImmune. In this position, he is responsible for new technology, antibody discovery, antibody/protein engineering, production cell line generation, structural biology and protein mimetics. He leads a global organization of about 160 scientists. He is actively involved in developing MedImmune's clinical- and preclinical-stage product candidates, and also participates in target discovery and validation for early research projects. He plays an essential role in discovering and developing an anti-RSV mAb, motavizumab that is currently under FDA review for market approval.

Dr. Wu has about 20-year experience in antibody discovery and protein engineering. He started as director, protein engineering and structure in MedImmune in 2002. Prior to joining MedImmune, he served as head, molecular biology department at Tanox, Inc. (acquired by Genentech in 2007). Before joining Tanox, he held a variety of research positions up to associate director, antibody engineering and discovery at Applied

Molecular Evolution (now a subsidiary of Eli Lilly & Co.). He is the recipient of the Senior Technology Fellow Emerald Honors award presented at the 2006 Minorities in Research Science Conference. He is also named as co-inventor on 9 issued patents and 42 patent applications related to antibody technology and antibody/protein therapy.

Dr. Wu received his bachelor's degree in chemistry from the National Taiwan University and his doctorate in molecular and cellular biology from the University of Massachusetts, Amherst. He completed his postdoctoral training at The Scripps Research Institute in La Jolla, California.

Honghui Zhou, Ph.D., FCP

Head, Pharmacokinetics, Modeling & Simulation, Centocor R&D, Johnson & Johnson, Pennsylvania, U.S.A.

Abstract

Pharmacokinetics/pharmacodynamics (PK/PD) of therapeutic proteins: what can we leverage from what we have learnt from small molecules?

Therapeutic proteins have played a crucial role in pharmacotherapy over the last decade and are projected to become increasingly more important. Several therapeutic monoclonal antibodies (mAb) have become therapies of choice in areas of oncology and immunology. During the life cycle of mAb development, PK/PD has played a crucial role in areas of dose selection, study optimization, product labeling, etc.

Great amount of knowledge and experiences have been accumulated from small molecule drug development over more than half a century. One recurring question often facing scientists in therapeutic protein drug development is: what we can leverage from what we have learnt in small molecules and apply them to the drug development of therapeutic proteins? This presentation is intended to briefly touch on differences between small molecules and therapeutic proteins, and address some unique challenges and corresponding strategies in drug development for therapeutic proteins from PK/PD perspective.

Biography

Honghui Zhou, Ph.D. is Senior Director at Centocor R&D where he is leading Pharmacokinetics, Modeling & Simulation Department for therapeutic biologics across Johnson & Johnson (J&J). Prior to joining J&J, Honghui also worked for Wyeth, Novartis, and J&J PRD in the area of clinical pharmacology for both small molecular drugs and therapeutic biologics.

Honghui has (co)-authored more than 100 original scientific manuscripts, book chapters and conference abstracts in the areas of pharmacokinetic/pharmacodynamic modeling, drug-drug interaction, absorption analysis, and therapeutic biologics. He has been an invited speaker in many national/international conferences (AAPS, NBC, ACCP, KSCPT-ASCPT, DIA, GRC, etc.) and FDA.

Honghui has been a Fellow of Clinical Pharmacology (FCP) at American College of Clinical Pharmacology (ACCP) since 1999. He is board certified by American Board of Clinical Pharmacology, and currently serves as Section Editor for Biologics for the *Journal of Clinical Pharmacology*. He has also been elected as Board of Regents of ACCP (2009-2014). He currently also serves as BIO liaison to PhRMA/FDA Drug Metabolism & Clinical Pharmacology, and co-chair FDA/Pharma Industry Biologics Drug-Drug Interaction Steering Committee.