**Morning Session: 08:00- 12:00**

08:00 - 08:15
**Welcome and Introduction**

08:15 - 09:00
**Topic #1:** New Trends in Regulatory Submissions – ICH Q8, Q9, Q10 and their impact on Product Development; Q and A

**Potential Speaker:** Dr. Ubrani V. Venkataram, Team Leader, Division of Chemistry II, Office of Generic Drugs, Food and Drug Administration

**Abstract:** The Pharmaceutical Development section in a regulatory submission such as an ANDA or NDA is intended to provide a comprehensive understanding of the drug product and its manufacturing process. The ICH Q8, Q9 and Q10 documents provide guidance for a systematic approach to developing and presenting such drug product and process understanding to regulatory authorities. These guidance documents, in conjunction with the CDER guidance document “Pharmaceutical CGMPs for the 21st Century – A Risk-Based Approach”, portray a vision of future pharmaceutical manufacturing that utilizes principles of Quality Systems and implements Risk-Based approaches. This presentation will provide an overview of these guidance documents as applicable to the development of Controlled Release Oral Dosage Forms.

09:00 - 09:45
**Topic #2:** Example Product Development Report Following New Regulatory Trends; Q and A

**Potential Speaker:** Dr. Yanning Lin, Senior Regulatory Chemistry Reviewer, Division of Chemistry II, Office of Generic Drugs, Food and Drug Administration

**Abstract:** The design and manufacture of complex dosage forms such as controlled release tablet formulation is quite challenging. The Office of Generic Drugs/FDA has published a 161 page example pharmaceutical development report of a controlled release tablet formulation, illustrating application of principles of Quality by Design (QbD) in product development. The QbD approach to product development leads to better product and process understanding and to lifecycle management and continual improvement. The talk will focus on elements of this QbD approach such as Quality Target Product Profile of the a controlled release tablet formulation by analysis of the innovator product, Risk

09:45 - 10:15
Break

10:15 - 11:00

Topic #3: Bioequivalence Approaches for Controlled Release Dosage Forms; Q and A

Potential Speaker: Dr. Xiaojian Jiang, Team Leader, Division of Bioequivalence II, Office of Generic Drug, Center for Drug Evaluation and Research, Food and Drug Administration

Abstract: Modified-release (MR) drug products contain excipients that control drug release rate. In approving a generic MR drug product, the FDA concludes that the generic product (test) is therapeutically equivalent, or switchable, with the corresponding brand product (reference). To be deemed therapeutically equivalent, the generic and reference product must demonstrate bioequivalence, that is, not show a significant difference in the rate and extent of drug absorption. The FDA requests several types of specialized bioequivalence studies for generic MR products. Bioequivalence studies are conducted in healthy subjects under both fasting and fed conditions. Food is studied because the performance of the release-controlling excipients can be altered when food changes the gastrointestinal tract (GI) environment. Thus, for a generic to be deemed bioequivalent to its reference, both products should have the same rate and extent of drug absorption in the presence of a high-fat, high-protein, high calorie meal, thought to be conditions most likely to cause maximal changes in the GI environment. If the reference product labeling gives the option of administering a MR product in soft food such as applesauce, then it is also necessary to show that the generic product is bioequivalent to the reference product when crumbled and mixed in soft food, ensuring that test and reference release-controlling excipients perform the same under these conditions. As some MR formulations may release drug substance rapidly in the presence of ethanol (“dose-dumping,” a potential safety issue) FDA also requests comparisons of test and reference drug in vitro dissolution rates in 0.1 N HCl media containing varying percentages of ethanol. Finally, for multiphasic MR products which contain an immediate-release component to provide rapid onset of therapeutic response, FDA requests bioequivalence metrics to confirm that test and reference drug exposure are equivalent over the early stages of the plasma concentration versus time profile.

11:00 - 11:45

Topic #4: A Development Strategy via IVIVR for Controlled Oral Solids Release Dosage Forms

Potential Speaker: Dr. Sherry Ku, President and CSO of TWi Biotech and TWi pharmaceutical Inc. (previously Anchen); Q and A

Abstract: Control Release Technology is a major tool to add value to a clinical compound. The value of oral once a day dosage form is far beyond improvement of compliance. Oral sustained release technology could be an enabling technology for narrow therapeutic window drug via reduction of drug blood concentration fluctuation, i.e. a lower Cmax/Cmin ratio. Enteric coating technology may also be an enabling technology for a drug with local GI irritation/intolerance. Injectable sustained technology is even of high value since the advent of large biomolecules that requires frequent injection. Reduction of invasive injection daily to monthly or quarterly or even yearly offers tremendous medical cost saving with a reduced risk of injection side effects. The trend of increasing large biomolecules has renewed interest in sustained injectable technology that new methodology is being invented vigorously. However, the development of a controlled release dosage form is frequently hampered by the lack of in-vitro in-vivo relationship. In other words, an in-vitro release rate over one week may last several
weeks in vivo or a faster release rate in vitro may prove a slower release in vivo. As a result, a large number of pilot human studies become necessary to find the right in-vitro release rate. Early delineation of in-vitro in-vivo relationship (IVIVR) is the only way to minimize costly human pilot studies and get to the final dosage form in an expeditious manner. The author will present a scheme in the early establishment of IVIVR based on compound solubility and permeability properties. This way a controlled release dosage form may be developed with 1 or 2 pilot human studies in a timeframe less than 6 months. The selection of controlled release technology based on target product profile (TPP) will also be described. This way the use of controlled release strategy to secure the maximum commercial life of a compound beyond its own chemical physical and biopharmaceutical properties may be employed effectively and efficiently.

11:45 - 12:00
Q and A with Morning Speakers

12:00 – 13:00
Lunch Break

Afternoon Session: 13:00 - 17:00

13:00 - 13:45
Topic #5: New trends and technology approaches for robust oral controlled release formulations; Q and A

Potential Speaker: Dr. Ali Rajabi-Siahboomi, VP & Chief Scientific Officer of Colorcon Inc.

Abstract: Oral controlled release (CR) continues to grow in all regions. There are significant efforts to shorten development cycle, enhance performance and ensure patient acceptability of the finished CR dosage forms. Various approaches are investigated to accommodate drugs of various dose, solubility and chemistry into well-known or new platform technologies. In addition, polymer combinations, co-processed excipients and new polymers are being developed and evaluated for delivering different release profiles, consistently and effectively. The presentation will review the most common oral CR technologies and approaches that have shown or being investigated to improve formulation and manufacturing robustness of these technologies.

13:45 - 14:30
Topic #6: The Use of Spectroscopic Methods for the examination of the Solid State of Controlled Polymers

Potential Speaker: Dr. Stephen Hoag, Professor of Pharmaceutical Sciences at University of Maryland

Abstract: The solid state of a polymer is critical to the dosage form performance, and spectroscopic methods such as NIR and Raman can be very useful for the investigation of the polymer-polymer and drug-polymer interactions that influence product quality. These interactions will be discussed using case studies from my research.

14:30 - 15:00
Break
**Topic #7:** A Backwards Look at Scale-up for the Wurster Process – Controlled Release Dosage Forms

**Potential Speaker:** Mr. David Jones, Founder and President of OWI-Consulting Inc. (Previously VP of Glatt Pharmaceutical Services)

**Abstract:** Product and process troubleshooting at the commercial scale is all but inevitable. Ideally, a process should be very straightforward so that it can quickly be evaluated as a potential root cause of the issue. This presentation begins with a review of electronic data for a commercial scale Wurster process (it is an example of ‘what not to do’). Several attributes are defined – step transitions; operating ranges (and operational qualification); major and minor excursions and critical process parameters. Next is a discussion of the benefits of DoE in process development at the laboratory scale. In the last segment, considerations for progressing to pilot and production scale are presented, including suggested process parameters.

**16:00 - 17:00**

Additional Time for Q and A; Adjourn
Biographies of the Workshop Speakers

Ubrani V. Venkataram, Ph.D.
Division of Chemistry II
Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration

Bio:
Ubrani Venkataram obtained a Ph.D. in Organic Chemistry from the Indian Institute of Science, India. After gaining post-doctoral experience, he joined Bristol-Myers Squibb as a Research Chemist where he conducted pre-formulation studies on several classes of drugs. He joined the Office of Generic Drugs/FDA as a Review Chemist in 1991. He is currently a Team Leader in the Division of Chemistry II. As a member of ICH CTD Expert Working Group, he was involved in the development of the Common Technical Document - Quality. He has published an article entitled “Common Technical Document – Quality (M4-Q): One Regulatory Participant’s Perspective” in Drugs and the Pharmaceutical Sciences – The Pharmaceutical Regulatory Process, Volume 144, page 547, Marcel Dekker publisher and I. R. Berry editor. He has given Chemistry, Manufacturing and Controls seminars at workshops to train generic industry regulators and scientists. He has conducted a workshop for reviewers in Jordan Food and Drug Administration. He was a member of the working group that was engaged in developing a mock QbD example for Extended-release Drug Products.

Sherry Ku, Ph.D.
President and CSO of TWi Biotech and TWi pharmaceutical Inc. (previously Anchen)

Bio:
Dr. M. Sherry Ku is the president and Chief Scientific Officer of TWi Biotech Inc. and TWi Pharma Inc. (Anchen Taiwan) since March, 2010. Under her leadership, TWi has filed 6 ANDA’s in the past 18 months encompassing oral controlled release dosage form and a hydrogel topical patch and an oral nanosuspension, each of which are of high technical barriers and/or paragraph IV patent challenges. During the same period, TWi Biotech filed US and Taiwan IND’s and conducted a Phase 2b multi-regional clinical trial (patient number= 259). Additional 3 NME US IND’s are scheduled for 2012. Previously as the head of Early pharmaceutical Development in Wyeth Research (now Pfitzer). Her responsibilities include discovery support, lead selection, phase 0 and IND submission until clinical proof of concept. With the recent trend of new clinical leads becoming less soluble with poor oral bioavailability, Sherry’s emphasis has been in drug delivery and solubilization technology. Since 2001, her group is responsible for the development of over 178 new clinical leads resulting in 85 initial IND filings. In this process, her department has become one of the key engines in the generation of intellectual properties (IP) for Wyeth. She currently holds over 42 published patents and a large number of invention disclosures and has additional 62 publications. Early on, Sherry developed seven (7) commercial products including Suprax, Zosyn/Tazocin, Zebeta, Isovorin, Thioplex, Sonata and most recently Tygacil encompassing discovery, development and tech transfer, validation, NDA filing and pre-approval inspection activities. She holds a Ph.D. Degree in Pharmaceutical Chemistry and Pharmaceutics from The Ohio State University and a B.S. degree in Pharmacy from National Taiwan University. She was the Vice Chair of NJ Pharmaceutical Discussion Group and is the Chair elect of AAPS Physical Pharmacy and Biopharmaceutical section. She sits on USP expert council and consults for sFDA, tFDA, IPEC and various Quality Councils.
**Ali Rajabi-Siahboomi, Ph.D.**  
VP & Chief Scientific Officer of Colorcon Inc.

**Bio:**  
Ali Rajabi-Siahboomi is Vice President and Chief Scientific Officer at Colorcon, based in Global Headquarter, USA. He obtained his B.Pharm. & PhD in Pharmacy from University of Nottingham (UK). Ali has held various academic positions in Nottingham and Liverpool JM Universities in the UK, before joining Colorcon as Technical Director, responsible for Europe, Middle East and Africa in 2000. His main research interests are in the area of solid dosage form pharmaceutics and pharmaceutical technology with emphasis on oral drug delivery systems. He has published over 200 articles, book chapters, abstracts and patents.

**Dr. Steven Hoag, Ph.D.**  
Professor of Pharmaceutical Sciences  
University of Maryland

**Bio:**  
Stephen W. Hoag, Ph.D., is a Professor of Pharmaceutical Sciences at the University of Maryland, Baltimore; he received his Ph.D. in Pharmaceutics from the University of Minnesota-Twin Cities and a B.S. in Biochemistry from the University of Wisconsin-Madison. Dr. Hoag has been a visiting professor at 3M Pharmaceuticals and Abbott Laboratories. His primary research interests are in the area of excipient functionality testing, QbD, tablet coating, coating polymers, tablet press instrumentation, tablet compaction modeling and formulation design. His research has included studies in formulation of folic acid in multivitamin and mineral supplements, formulation of botanical products, controlled release formulation, polymer science, pigment stability in coating polymers and thermal analysis of polymers, powder flow and formulation stability. In collaborated with the Center for Veterinary Medicine division of the FDA, Hoag has studied the application of near infrared spectroscopy to the analysis of excipient identification, tablet quality and production monitoring for process analytical technology (PAT) applications. Working with Dr. Larry Augsburger, he has edited a three volume set of books on tablet compaction. Dr. Hoag is a member of NIPTE (National Institute of Pharmaceutical Technology and Education) Executive Committee, he has been elected to the USP Counsel of Experts and he is an AAPS fellow. In addition, he serves on the International Steering Committee for the Handbook of Pharmaceutical Excipients and he serves on the editorial board of the journal of Pharmaceutical Development Technology.

**Mr. David Jones**  
Founder and President of OWI-Consulting Inc.  
(Previously VP of Glatt Pharmaceutical Services)

**Bio:**  
July, 2008 – present: OWI-Consulting Inc  
Founder and President  
- Specializing in all aspects of fluidized bed processing, from lab to pilot to production; submission batch manufacturing; process troubleshooting for marketed products; operator and staff training; MBR, SOP, protocol writing  
Vice President, Process Technology  
- Processing consultant to Formulation Development Department at Glatt Air Techniques, Inc.  
- Write protocols, master batch records and summary reports for all aspects of processing, including submission batch manufacture. Conduct or supervise batch processing in-house or at client site.  
- Internationally recognized in the field of multi-particulate dosage forms for modified release.
- Processing consultant for multi-national branded and generic companies for equipment start-up, scale-up, tech transfer and process troubleshooting (globally), including some of the top selling drugs in the world.
- Member of Orocel Team, Glatt's global product development group headquartered in Binzen, Germany.
- Inventor of Glatt's Wurster HS technology for pelletizing and particle coating; coinventor of STRATOS air suspension tablet coating; tangential spray powder layering; product-by-process for pelletizing in CPS technology.
- Invited speaker for AAPS National and Regional meetings; EPTM, ISPE, NJ and Philadelphia Discussion Groups, AIChE, Controlled Release Society, Glatt's TTC (Technology Training Center), FDA (OGD, CDER).
- Course organizer and director for annual Glatt Process Training and Formulation Seminars.
- Organizer and course director for client-site process training seminars for operators and professional staff at branded and generic companies.

Other positions held at Glatt include Laboratory Manager; Director, International Process Technology Development; Executive Director, Scientific Affairs.

Patents Issued patents: 6,911,087; 6,695,919; 6,692,571; 6,579,365; 5,437,889; 5,236,503; 5,132,142. Wurster HS; air suspension tablet coating; pelleting by powder layering. 3 patents pending (CPS pelletizing technology).

Numerous publications in various industry trade journals including PharmTech Magazine. Five book chapters in Marcel-Dekker publications.

1971 – 1978 University of Delaware, Newark, Delaware Electrical and Mechanical Engineering; Business

**Xiaojian Jiang, Ph.D.**

Team Leader of the Division of Bioequivalence II

Office of Generic Drugs, CDER, FDA

**Bio:**

Dr. Xiaojian Jiang is currently serving as the Team Leader of the Division of Bioequivalence II, in the Office of Generic Drugs, CDER, FDA. As such, Xiaojian supervises, manages and oversees the Team 7 review of clinical bioequivalence trial data submitted to Abbreviated New Drug Applications for marketing approval of new generic drug products pertaining to locally-acting Gastrointestinal (GI) drugs, Antibiotics, Anti-Parkinson drug products, etc. Since March 2009, Xiaojian has led the review team 7 on developing novel BE approaches for evaluating challenging locally acting GI drugs including vancomycin capsules, mesalamine oral products, orlistat capsules using in vitro BE study method and pharmacodynamic endpoint study.

Xiaojian joined the Division of Bioequivalence in 2003. As a Senior Pharmacology Reviewer in the Division of Bioequivalence, she successfully reviewed numerous ANDAs, amendment, supplements, protocols, control documents and DSI inspection reports. Throughout this year, she has developed in-depth understanding and expertise in the area of BE approaches and generic drug approval process. She also made significant contributions to several guidance developments and various FDA working groups to resolve complex regulatory issues. From Nov. 2007 to Feb. 2009, she served as a dissolution expert in the DB. Her primary role was to provide consultation to DB reviewers pertaining to complicated in vitro dissolution issues. She has received several FDA and CDER awards due to her outstanding quality work and significant contributions to the FDA and CDER initiatives. She also had multiple presentations and publications in the area of BE approaches for locally acting drug products,
issues related to the highly variable drug products, in vitro dissolution testing, in vitro BE approach for Nasal Spray Product, and metabolite determination in BE studies, etc.

Xiaojian received his Ph.D. in Pharmaceutical Sciences from the University of Maryland, Baltimore. Her thesis work focused on developing of a Novel Liquid Sustained-Release Drug Delivery System for Water-soluble Drugs. She had two Patents related to her thesis work.

Yanning Lin, Ph.D.
Division of Chemistry II
Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration

Bio:
Yanning Lin obtained a Ph.D. in Industrial Pharmacy from School of Pharmacy, University of Maryland at Baltimore under the supervision of Dr. Larry L. Augsburger and a Master degree in Organic Synthesis from Department of Chemistry, Illinois State University. After obtaining her Ph.D. in Industrial Pharmacy and Co-op work at Warner-Lambert/Parke Davis (current Pfizer), she worked in Wyeth Research (current Pfizer) and generic companies in preformulation studies, formulation development, process development, and technical support for diverse pharmaceutical dosage forms: tablets, capsules, and liquid for 8 years to support Investigational New Drug (IND) filings to FDA, to lead and manage multiple projects involving multi-disciplinary groups, with 10 published papers and posters and 5 published and pending US patents. She joined the Office of Generic Drugs/FDA as a Review Chemist in 2008. Currently, she is a Senior Review Chemist in the Division of Chemistry II to review Abbreviated New Drug Applications (ANDA) in Office of Generic Drugs, Food and Drug Administration.