・10/5～7，出席した専門家会議

“科学とリスクに基づく医薬品の品質評価専門家会議”(Maryland 州, White Filint, Marriott Hotel North Bethesda)
外国旅行記録書別添資料１としてプログラムを示す.

・10/11～12，訪問先及び面接者

米国食品医薬品局医薬品評価研究センター（CDER, Maryland 州，Rockville）

Mr. Gary Buehler
Director
Office of Generic Drugs

Dr. Lawrence X. Yu
Director for Science
Office of Generic Drugs

Dr. Frank O. Holcombe
Associate Director for Chemistry
Office of Generic Drugs

Dr. Guirag Poochikian
Director
Office of New Drug Quality Assessment

Dr. Chi-wan Chen
Deputy Director
Office of New Drug Chemistry

Dr. Rajendra Uppoor
Pharmacist, Policy Development Staff
Office of Pharmaceutical Science

４．成果

（１）米国食品医薬品局研究所訪問（10/4），Division of Product Quality Research, White Oak Life Science Building, Silver Spring, Maryland

米国行政研究機関における医薬品等の品質確保やその基準の設定に必要な技術的アプローチについて，意見交換を行った．訪問先はUS-FDAに属する部門の１つであるDivision of Product Quality Research であり，Maryland 州の Silver Spring に位置している．この Division では，Chemistry team, Physical pharmacy team, Biopharmaceutics team から構成されている．はじめに Division of Product Quality Research の Director である Dr. Monsoor Khan から研究所の業務内容について紹介があり，研究のキーワードとして，Support, Policy, Safety, Industrization, Post market, Risk management が挙げられ，Research → Regulatory Policy → Review and Regulation→Research のサイクルを柱とした，「安全性と有効性を評価及び予測のため，また医薬品，生物製剤又は機器における新規のアイデアを生み出すための“科学とは趣の異なる製造を可能とさせるために必要な科学”」と表現される”Critical Path” Research の紹介があった.

次いで，この Critical Path Research に基づいて研究を行っている３つのチームについてそれぞれ説明があった．Chemistry Team からは Team leader の Dr. Patrick Faustino から，Prussian Blue を用いた医薬品の安全性，有効性に関する研究について，また Frosemide を用いた溶出性の研究などが紹介された．Physical Pharmacy Team からは Team Reader の Dr. Everett Jefferson から，Process Analytical Technology (PAT)への応用を目指した近赤外分光分析 (NIR)，ラマン分光分析及びそれらのイメージング等を用いた研究について，特に混合均一性や錠剤及びカプセル剤における主薬及び添加剤のマッピングと定

量予測や Frosemide 錠を用いた NIR スペクトルと溶出性の相関研究に関する成果について紹介された．Bio-pharmaceutics Team からは Team Reader の Dr. Donna A. Valpe から薬物の溶解性と腸吸収性を基に薬物を分類する BCS guidance に関して，特に添加剤の薬物動態学的影響に関する研究及び生物学的同等性に関する研究について紹介された．また，当部門で業務として進めている Pharmaceutical Chemistry Program として，Chemistry，Guidance Support，OPS rapid response，PAT Projects 及び Regulatory Project が挙げられ，これらの関して関連部門との密接な連携をとっていることも紹介された．

一方で，我が国における当該研究に関する状況を説明し，今後の両機関における研究協力体制のあり方についても併せて意見交換を行った．また，特殊な剤形をもつ製剤の 1 つとして経皮吸収製剤の品質評価のあり方に関する意見交換を行った．

これら種々の剤形における医薬品の品質確保に関する研究について，US-FDA における最新の動向並びに今後の研究のあり方を調査することにより，我が国における経皮吸収製剤の品質確保のあり方に有用な情報を得ることができた．

（2）US-FDA，ISPE 及び米国薬学会共催ワークショップ，科学とリスクに基づく医薬品の品質評価会議出席（10/5～10/7）

本ワークショップは，US-FDA が中心として医薬品の品質保証のあり方や展望に関する討論を行う世界規模の専門家会議であり，世界各国から約 400 名の医薬品規制当局関係者及び製薬会社品質保証関係者らが集まり，主要国における医薬品の品質に関するトピックの講演やテーマごとの専門家会議による討論が行われた．全体のプログラムは外国旅行記録書別添資料 1 に示すが，「新たな品質システム（パラダイム）を具体的に運用するための規制当局と申請者（企業）がどのように共通の認識をもつべきか」という目的に合わせて，US-FDA，EU，日本及び企業団体より基本概念やそれに対する取り組みの現況に関する講演の後，専門家会議として，（A）製剤開発（Pharmaceutical Development, PD）：製剤開発に含まれる情報，含まれる情報により生じる利益・不利益，PD 資料の提出・審査のあり方について，（B）CMC 規制プロセス（CMC Regulatory Process）：申請及び審査プロセス業務の効率化について，(C) CMC 規制に関する合意：申請・登録事項について，また審査完了後の CMC 規制に関する合意・契約について，(D) コミュニケーション（Communication）：製品のライフサイクルを通じての申請者－規制当局間のコミュニケーション，知識の共有のための新しい考え方，（E）デザインスペース（Design Space, DS）：定義・開発・記述のあり方と審査・承認の実際と更新について，（F）QbD（Quality by Design）の工程操作への適用：事例研究（Wyeth Research の徐放性錠剤開発における QbD の事例と Abbott における錠剤の質量管理の事例紹介と考察），（G）QOS（Quality Overall Summary，概要資料）：審査の効率化を向けた概要資料の導入とそのあり方について，（H）革新と継続的な改善：近代的な医薬品品質システムにおける“継続的な改善”のあり方と“科学とリスクに基づいた医薬

品評価”が“継続的な改善”に対して与える影響について，(I) 市販後の変更管理：新たなパラダイムでの市販後変更管理（評価）の医薬品の評価における役割について，(J) 医薬品の審査と GMP 査察の統合：医薬品の CMC 審査と GMP 査察の統合について，(K) 医薬品評価の実際：新たなパラダイムに向けて提案された QbD に対する規制当局における審査のあり方と効率的な CMC 審査を達成させるために何をすべきか，(L) QbD の工程操作への適用：事例研究（Schering-Plough Research Institute における原薬合成への適用事例と Glaxo Smith Kline における PAT/QbD の導入事例，及び考察）（以上，外国旅行記録書別添資料２に示す）が開催され，テーマごとに専門家が集まり，質疑応答及び討論が行われた．

これらのテーマについて，“新しいパラダイムの下で経皮吸収製剤の品質保証のあり方をどのようにするべきか”という点を中心に会議に出席した専門家と意見を交わした．

（３）US-FDA 医薬品評価研究センター（CDER, Maryland 州，Rockville）訪問（10/11～12）

US-FDA CDER の新薬及び後発医薬品の審査並びに GMP 査察の専門官から種々の医薬品における品質基準や品質試験検査の評価に対する具体的な考え方について意見交換を行った．両日のスケジュールは外国旅行記録書別添資料３に示したとおりである．

Office of Generic Drugs (OGD)では，Director の Mr. Gary Buehker より最近の米国における後発医薬品の申請状況と品質保証の動向について説明を受けた．この中で，特に最近における後発医薬品の申請件数の著しい増大と原薬の第三国からの輸入量の増大による品質確保の新しい局面を迎えている状況であることが注目するべき内容であった．続いて，Associate Director for Chemistry である Dr. Frank Holcombe より後発医薬品における CMC 審査の実際について，特に生物学的同等性に関する審査のポイントについて説明を受けた．一方で，Director for Science である Dr. Lawrence Yu と Science Team(Question-based Review Group)のメンバーらと後発医薬品の CMC 審査の対象データと審査のアプローチに関する意見交換を行った．この中で，今後申請時に提出される CMC 資料について，米国が現在考えている“概要（Quality Overall Summary）”を基に，医薬品の品質（“規格及び試験方法”）に対する妥当性の検証を行うアプローチの紹介があり，この点に関する日本における“概要”の承認申請資料としての位置付けと意義並びに“規格及び試験方法に対する技術的審査ポイント”について説明し，科学的観点からの今後の後発医薬品の CMC 審査のあり方について意見交換を行った．また，同グループにおける後発医薬品の CMC 審査に対する支援研究に関する紹介を受け，日本における行政支援研究の現状と今後の検討課題について意見交換を行うとともに双方で共通の認識をもっていることを確認し，今後とも情報交換を継続していくこととなった．

Office of New Drug Quality Assessment (ONDQA)では，Director である Dr. Guirag

Poochikian 及び Office of New Drug Chemistry の Deputy Director である Dr. Chi-wan Chen から，新医薬品の承認審査の流れと最近の承認審査の動向について説明を受けた．また，最近の US-FDA における経皮吸収製剤の CMC 審査のポイントについて説明を受け，ICH の品質に関連するトピックの動向を考慮した企業における経皮吸収製剤の開発研究や規制当局における CMC 審査のあり方について討議を行った．

Office of Pharmaceutical Science (OPS) では，Dr. Rajendra Uppoor より CDER における OPS の役割や US-FDA における cGMP の今後の方向性などの説明を受けた後，日本における改正薬事法による承認システムや GMP 査察体制の変化について説明をし，今後の GMP 査察のあり方に関する双方のヴィジョンについて意見交換を行ったほか，医薬品等査察官の教育訓練のあり方について，両国における具体的な教育訓練のシステムに関する情報交換も併せて行った．特に経皮吸収製剤については，一般的な内服製剤と異なる特殊な剤形をもつことから製造及び品質管理における特有のポイントもあり，これらについて GMP 適合性の観点から意見交換を行った．

今回の US-FDA への訪問と“科学とリスクに基づく医薬品の品質評価専門家会議”に出席し，米国も含めた各国の規制当局及び企業の経皮吸収製剤の専門家と技術的な意見交換を行うことにより，経皮吸収製剤の品質確保の国際的動向について把握することができた．また経皮吸収製剤の品質確保のあり方について，本研究の今後の方向付けを行うことができた．

（外国旅行記録書別添資料１）

AAPS Meetings and Expositions

AAPS Workshop on Pharmaceutical Quality Assessment - A Science and Risk-based CMC Approach in the 21st Century
Co-sponsored with FDA and ISPE

October 5 - 7, 2005

Bethesda North Marriott

North Bethesda, Maryland

Features:

KEY Program

Goals and Objectives

Consistent with the CGMPs for the 21st Century Initiative, FDA is establishing a modern, risk-based pharmaceutical quality assessment system to replace the current chemistry, manufacturing, and controls (CMC) review system. The new quality assessment system is intended to facilitate innovation and continuous improvement throughout the product lifecycle and to provide regulatory flexibility for specification setting and post-approval changes based on scientific knowledge and understanding of product and process by applying quality-by-design principles and to expedite the review of drug applications without compromising the high quality of drugs in the United States. Plenary sessions will present scientific and technical challenges to provide the framework for discussions in the breakout sessions. Breakout sessions will serve as the forum for FDA to seek input from the public in understanding the pros and cons of the various aspects and in identifying alternative approaches to achieve the desired state. Specifically, the workshop will:

- explore and evaluate all facets of the new pharmaceutical quality assessment system;
- define what is meant by a risk-based system and how to establish criteria to identify and measure risk associated with the development and manufacturing of pharmaceutical drug products;
- assess the roles and value of Pharmaceutical Development Information, Quality Overall Summary, and integrated review/inspection functions in the new paradigm;
- examine the kind, amount and extent of data in future CMC submissions and its value in making

science-based regulatory decisions;

- develop appropriate strategies to submit and to assess critical manufacturing science information to facilitate PAT, and to encourage innovation in pharmaceutical manufacturing;
- determine how to set product specifications in the new paradigm based on recommendations and findings of PQRI Workshop (March 2005); and
- identify the roles of industry and FDA to facilitate continuous product and process improvement.

Desired Outcomes

In addition to providing a better understanding of the critical elements of the new regulatory system, this workshop will provide the following:

- identification of scientific training gaps that must be filled for the successful implementation of the new system;
- industry input to FDA to influence the establishment of a scientific risk-based regulatory system that maintains high quality and facilitates continuous improvement;
- help determine implementation strategies on how to utilize pharmaceutical development information and quality overall summary in the new system (submission and review);
- identify the roles and responsibilities of industry and regulators in the new paradigm;
- a written document that could serve as the basis for development of regulatory guidance; and
- propose ways to reduce the number of post-marketing supplements.

Workshop Agenda

Wednesday, October 5

7:00 am · 5:00 pm

Foyer Ballroom C Registration

8:30 am · 10:15 am Ballroom A-D

Session I: Workshop Goals and Objectives

Moderator

Helen Winkle

U.S. Food and Drug Administration

8:30 am · 8:45 am

Introductory Remarks · Purpose of Workshop and Goals

Helen Winkle

U.S. Food and Drug Administration

8:45 am

Pharmaceutical Quality in the 21st Century · An Integrated System Approach

Janet Woodcock, M.D.

U.S. Food and Drug Administration

9:15 am

A New Pharmaceutical Quality Assessment System (PQAS) for the 21st Century ・Why is it Needed, What Does it Mean, and How Do We Get There?

Moheb M. Nasr, Ph.D.

U.S. Food and Drug Administration

9:45 am

Understanding Key Terms for Modern Quality Assessment

John E. Simmons, Ph. D.

U.S. Food and Drug Administration

10:15 am

Coffee Break

10:30 am ・12:10 pm Ballroom A-D

Session II: Quality by Design (QbD) ・Integration of Prior Knowledge and Pharmaceutical Development into CMC Submission and Review

Moderator

John C. Berridge, Ph.D.

Pfizer Inc.

10:30 am

FDA Perspective

Ajaz S. Hussain, Ph.D.

U.S. Food and Drug Administration

11:00 am

Industry Perspective

John C. Berridge, Ph.D.

Pfizer Inc.

11:30 am

Design Space and Regulatory Flexibility ・A Way Forward

Chris J. Potter, Ph.D.

AstraZeneca

11:50 am

Incorporating the Concepts of Quality-by-Design in the Assessment of Generic Drugs

Gary J. Buehler, R.Ph.

U.S. Food and Drug Administration

12:10 pm ・1:15 pm Ballrooms E-H

Lunch

1:15 pm ・2:15 pm

Concurrent Breakout Sessions and Case Studies

A. Pharmaceutical Development (PD): What information could be included in PD? What are the advantages and disadvantages of including PD in submission? How should PD be submitted and reviewed? *Ballroom A*

Moderators:

Chi-Wan Chen, Ph.D., U.S. Food and Drug Administration

Karen B. Main, Ph.D., AstraZeneca

Jean-Louis Robert, Ph.D., Laboratoire National de Sante, Service du Contr · e des Medicaments, Luxembourg

B. CMC Regulatory Processes: How can we make a dual/broad spectrum of submissions and review processes work effectively? *Ballroom B*

Moderators:

Jon E. Clark, U.S. Food and Drug Administration

Elizabeth A. Ernst, Roxane Laboratories

Diane J. Zezza, Ph.D., Schering Plough Corporation

C. CMC Regulatory Agreement: What are application/registration commitments and how can the FDA establish a CMC regulatory agreement/contract after the review is completed?*Ballroom C*

Moderators:

Moheb M. Nasr, Ph.D., U.S. Food and Drug Administration

Patricia C. Tway, Ph.D., Merck & Company, Inc.

Nirdosh Jagota, Ph.D., Wyeth

D. Communication: Can we find new ways for knowledge sharing and communication between industry and the U.S. FDA throughout the product lifecycle? *Ampitheater*

Moderators:

Helen Winkle, U.S. Food and Drug Administration Douglas Ellsworth, U.S. Food and Drug Administration Jeffrey J. Blumenstein, Ph.D., Pfizer Inc. Gordon Johnston, GPhA

E. Design Space: How is design space defined, developed and described? How is it reviewed and approved? How can it be updated post approval?*Forest Glen*

Moderators:

Ajaz S. Hussain, Ph.D., U.S. Food and Drug Administration

Scott Reynolds, Ph.D., Merck & Company, Inc.

Chris Potter, Ph.D., AstraZeneca

Susanne Keitel, Ph.D., Federal Institute for Drugs and Medical Devices, Bonn

F. Implementation of QbD Principles into Unit Operations - Case Studies

Glen Echo and Ballroom D

Moderators:

Charles P. Hoiberg, Ph.D., Pfizer Inc.

Steve Poehlein, Ph.D., Merck & Company, Inc.

2:30 pm

Concurrent Breakout Sessions Repeated

3:30 pm

Coffee Break 3:45 pm

Concurrent Breakout Sessions Repeated 5:00 pm - 6:00 pm Reception

Thursday, October 6

7:30 am - 5:00 pm Foyer of Ballroom C Registration

8:00 am - 9:30 am Ballrooms A-D

Session III: Breakout Session Reports (A-E)

Moderator

Moheb M.

Nasr, Ph.D. U.S. Food and Drug Administration

8:00 am Introductory Remarks

Moheb M. Nasr

Ph.D. U.S. Food and Drug Administration

8:15 am

Breakout Session A Report

8:30 am

Breakout Session B Report

8:45 am

Breakout Session C Report

9:00 am

Breakout Session D Report

9:15 am

Breakout Session E Report

9:30 am - 10:35 am Ballrooms A-D

Session IV: Utilization of Comprehensive Quality Overall

Summary (QOS) in CMC Submission and Review

Moderator

Guirag K. Poochikian

Ph.D. U.S. Food and Drug Administration

9:30 am

FDA Perspective

Guirag K. Poochikian, Ph.D.

U.S. Food and Drug Administration

9:50 am

International Perspective

Yukio Hiyama, Ph.D.

National Institute for Health Sciences, MHLW, Japan

10:05 am

International Perspective

Gary Condran

Health Canada

10:20 am

Industry Perspective

James V. McArdle, Ph.D.

Isis Pharmaceuticals

10:35 am

Coffee Break

10:50 am ・12:20 pm Ballrooms A-D

Session V: Innovation and Continuous Improvement ・Challenges and Opportunities

Moderator

Gerald P. Migliaccio

Pfizer Inc.

10:50 am

G.K. Raju, Ph.D.

Raju (PDF)

Massachusetts Institute of Technology

11:20 am

George P. Millili, Ph.D.

Millili (PDF)

Johnson & Johnson

11:50 am

Gerald P. Migliaccio

Pfizer Inc.

12:20 pm - 1:30 pm Ballrooms E-H

Lunch

1:30 pm - 2:30 pm

Concurrent Breakout Sessions and Case Studies

G. Quality Overall Summary (QOS): Can QOS be used as an effective review tool? What information in QOS is useful to the reviewer?*Ballroom A*

Moderators:

Norman Schmuff, Ph.D., U.S. Food and Drug Administration

Richard P. Poska, M.S., Abbott Laboratories

Yukio Hiyama, Ph.D., National Institute for Health Sciences, MHLW, Japan Gary Condran, Health Canada

H. Innovation and Continuous Improvement: How can a modern pharmaceutical quality system promote continuous improvement? How can scientific risk-based pharmaceutical assessment facilitate continuous improvement? *Ballroom B*

Moderators:

Christine M. Moore, Ph.D., U.S. Food and Drug Administration

Joe Famulare, U.S. Food and Drug Administration

Tim Marten, D.Phil., AstraZeneca

John C. Berridge, Ph.D., Pfizer Inc.

I. Post-marketing Changes (Supplements / Variations): What is the role of pharmaceutical assessment in the evaluation of post-marketing manufacturing changes in the new paradigm? Why is it needed and what for? *Ballroom C*

Moderators:

Eric P. Duffy, Ph.D., U.S. Food and Drug Administration

Leo J. Lucisano, GlaxoSmithKline Sue Schniepp, Hospira

J. Integration of Review and Inspection: How can we build synergy between CMC review and inspection? *Ampitheater*

Moderators:

Keith Webber, Ph.D., U.S. Food and Drug Administration

David J. Horowitz, Esq., U.S. Food and Drug Administration

Neil Wilkinson, Ph.D., AstraZeneca

John Franolic, Ph.D., Lachman Consultant Services, Inc.

K. Pharmaceutical Assessment Practices: What are the critical elements required for successful regulatory assessment of Quality-by-Design applications submitted in the new paradigm? What can we do to ensure a smooth transition to a new regulatory CMC assessment?*Forest Glen*

Moderators:

Lawrence Yu, Ph.D., U.S. Food and Drug Administration

Diane J. Zezza, Ph.D., Schering Plough Corporation

John Kovaleski, Teva Pharmaceuticals

L. Implementation of QbD Principles into Unit Operations - Case Studies

Glen Echo and Ballroom D

Moderators

Charles P. Hoiberg, Ph.D., Pfizer Inc.

Steve Poehlein, Ph.D., Merck & Company, Inc.

2:30 pm

Coffee Break

2:45 pm

Concurrent Breakout Sessions Repeated

4:00 pm

Concurrent Breakout Sessions Repeated

Friday, October 7 7:30 am - 12:00 pm Foyer of Ballroom C

Registration

8:00 am Ballrooms A-D

Introductory Remarks

Patricia C. Tway,Ph.D.

Merck & Company, Inc.

8:15 am - 9:15 am

Challenges and Opportunities in Drug Development, Manufacturing, and Regulations

8:15 am

U.S. FDA Perspective

Steve Galson, M.D.

U.S. Food and Drug Administration

8:45 am

Industry Perspective

Richard C. Clark

Merck & Company, Inc.

9:15 am

Breakout Session G Report

9:30 am

Breakout Session H Report

9:45 am

Breakout Session I Report

10:00 am

Breakout Session J Report

10:15 am

Breakout Session K Report

10:30 am

Breakout Sessions F and L Reports (Case Studies)

10:50 am

Coffee Break

11:10 am

Workshop Summary and Panel Discussion

Moderators

Moheb M. Nasr, Ph.D., U.S. Food and Drug Administration

Patricia C. Tway, Ph.D., Merck & Company, Inc.

Helen Winkle, U.S. Food and Drug Administration

Panelists:

Nicholas Cappuccino, Ph.D., Andrx Corporation

Chi-Wan Chen, U.S. Food and Drug Administration

Douglas Ellsworth, U.S. Food and Drug Administration

Yukio Hiyama, Ph.D., National Institute for Health Sciences, MHLW

Japan Steve Poehlein, Ph.D., Merck & Company, Inc.

Jean-Louis Robert, Ph.D., Laboratoire National de Sante, Service du Controle des Medicaments, Luxembourg

12:00 pm

Adjournment

2:30 pm

Coffee Break

2:45 pm

Concurrent Breakout Sessions Repeated

4:00 pm

Concurrent Breakout Sessions Repeated

Friday, October 7 7:30 am • 12:00 pm Foyer of Ballroom C

Registration

8:00 am Ballrooms A-D

Introductory Remarks

Patricia C. Tway,Ph.D.

Merck & Company, Inc.

8:15 am • 9:15 am

Challenges and Opportunities in Drug Development, Manufacturing, and Regulations

8:15 am

U.S. FDA Perspective

Steve Galson, M.D.

U.S. Food and Drug Administration

8:45 am

Industry Perspective

Richard C. Clark

Merck & Company, Inc.

9:15 am

Breakout Session G Report

9:30 am

Breakout Session H Report

9:45 am

Breakout Session I Report

10:00 am

Breakout Session J Report

10:15 am

Breakout Session K Report

10:30 am

Breakout Sessions F and L Reports (Case Studies)

10:50 am

Coffee Break

11:10 am

Workshop Summary and Panel Discussion

Moderators

Moheb M. Nasr, Ph.D., U.S. Food and Drug Administration

Patricia C. Tway, Ph.D., Merck & Company, Inc.

Helen Winkle, U.S. Food and Drug Administration

Panelists:

Nicholas Cappuccino, Ph.D., Andrx Corporation

Chi-Wan Chen, U.S. Food and Drug Administration

Douglas Ellsworth, U.S. Food and Drug Administration

Yukio Hiyama, Ph.D., National Institute for Health Sciences, MHLW

Japan Steve Poehlein, Ph.D., Merck & Company, Inc.

Jean-Louis Robert, Ph.D., Laboratoire National de Sante, Service du Controle des Medicaments, Luxembourg

12:00 pm

Adjournment

Notes

Please note the correction to the title for Breakout Session I should be 'Post-marketing Changes' not 'Post-manufacturing Changes' as indicated in the preliminary program.

（外国旅行記録書別添資料２）

BREAKOUT SESSION A: Pharmaceutical Development

Moderators: Chi-Wan Chen, Ph.D., FDA; Karen B. Main, Ph.D., AstraZeneca; Jean-Louis Robert, Ph.D., EU

Focus:

Pharmaceutical development information in the New Drug Application has been, traditionally, limited. ICH is in the process of establishing Q8 *Guidance on Pharmaceutical Development* to provide a high-level framework (Part 1) and further technical guidance (i.e., the proposed Part 2 on select dosage forms and Part 3 on drug substances) on what information to be included in the P.2 section, Pharmaceutical Development (PD). This breakout session will examine the information suitable for inclusion in the PD and the utility of PD in regulatory assessment.

Questions:

1. What information could or should be included in the Pharmaceutical Development (PD) Section?

    - How can the industry utilize ICH Q8 *Guidance on Pharmaceutical Development*? Is more guidance needed (in addition to Parts 2 and 3)? In which areas?
    - What type of information would the industry provide in PD? What information does the FDA expect to see and when?
    - What is the value of including failed experiments and optimization studies?
    - Can there be a difference between different dosage forms? How?

2. How should information in PD be submitted and reviewed?

    - Is a summary report adequate or should actual data be submitted?
    - How does the applicant include information from prior submissions, general references, or literature?
    - What are the industry's expectations and/or concerns for the regulatory review of PD? What are the FDA's expectations and/or concerns for reviewing PD?
    - Can PD form the basis for post-approval changes? How?

Deliverables:

Recommendations on: (1) what type of information could or should be included in PD; and (2) how information should be submitted and reviewed.

BREAKOUT SESSION B: CMC Regulatory Processes

Moderators: Jon Clark, FDA; Elizabeth Ernst, Roxane Laboratories; Diane Zezza, Ph.D., Schering Plough Corporation

Focus:

Discussions in this breakout session should propose recommendations to assure that a regulatory process is in place to adequately review and approve the broad spectrum of applications that may result in the new paradigm. Mechanisms for clearly communicating expectations for each type of application should be identified. The role and value of guidances in the new paradigm should be determined.

Questions:

1. What are the expectations for content across the different types of applications (i.e. Quality-by-Design principles vs. current standards)? How are these expectations communicated?

2. How do you know what type of application you have? How and when is this aligned and communicated across FDA and industry? What if my application is a hybrid application (i.e. Quality-by-Design DP, current standard DS)? How can you envision having an approved standard application and transitioning to a Quality-by-Design application?

3. What is the role of guidances? Do we need new or different guidances? What do we do with existing guidances? How does a reviewer apply the recommendations across different guidances (i.e. draft Drug Product Guidance vs. PAT Guidance) and draw the same conclusions?

4. Do the different types of applications require different expertise at the level of the reviewer? What are the options for training? How will the review be affected and is there a possibility to generate deficiencies and result in approvability issues?

Deliverables:

Specific recommendations for developing effective review processes to accommodate the broad spectrum of submissions that will result in the new paradigm.

BREAKOUT SESSION C: CMC Regulatory Agreement

Moderators: Moheb Nasr, Ph.D., FDA; Patricia Tway, Ph.D., Merck;
Nirdosh Jagota, Ph.D., Wyeth

Focus:

The rationale for having a regulatory agreement is to encourage sponsors to share scientific information, which will increase flexibility for regulatory strategy. The agreement will define the boundaries of the design space and will include binding CMC elements (critical process parameters, critical quality attributes, specifications, etc.). The changes within the design space can be implemented by the sponsor within the quality systems of the manufacturing plant. Some of these quality system principles could be addressed in ICH Q 10. The regulatory agreement document can be used by FDA investigators as a basis for pre-approval inspection.

Questions:

1. Does the audience agree with the general concept of the 'Regulatory Agreement'? What are the potential elements of this Regulatory Agreement? Would this approach address industry concerns about application commitments? What is its value to the agency reviewers and inspectors?

2. What is the regulatory process and timing for FDA/industry to reach an agreement? How will the agreement be implemented by the center and field? How to cover for changes which are not part of the formal 'Regulatory Agreement?

3. What are the challenges of implementation? How can FDA and industry work together to make this happen?

4. Can this concept be used only for those applications which are based upon 'Quality by Design' or for all applications?

5. Can this approach be applied to existing marketed products?

6. How can a sponsor modify 'Regulatory Agreement' post-approval?

7. Which section of the CTD is appropriate for submitting 'Regulatory Agreement'?
    - Module 1
    - 3.2.P.2 (Pharmaceutical Development) conclusion section
    - 'QOS' Quality overall Summary
    - New section for 'Regulatory Agreement'
    - Other?

Deliverables:

The breakout session will focus on obtaining FDA/industry consensus on the concept and implementation plan for 'Regulatory Agreement'. Consensus will also be sought on the scope of Regulatory Agreement and its applicability to new and existing products.