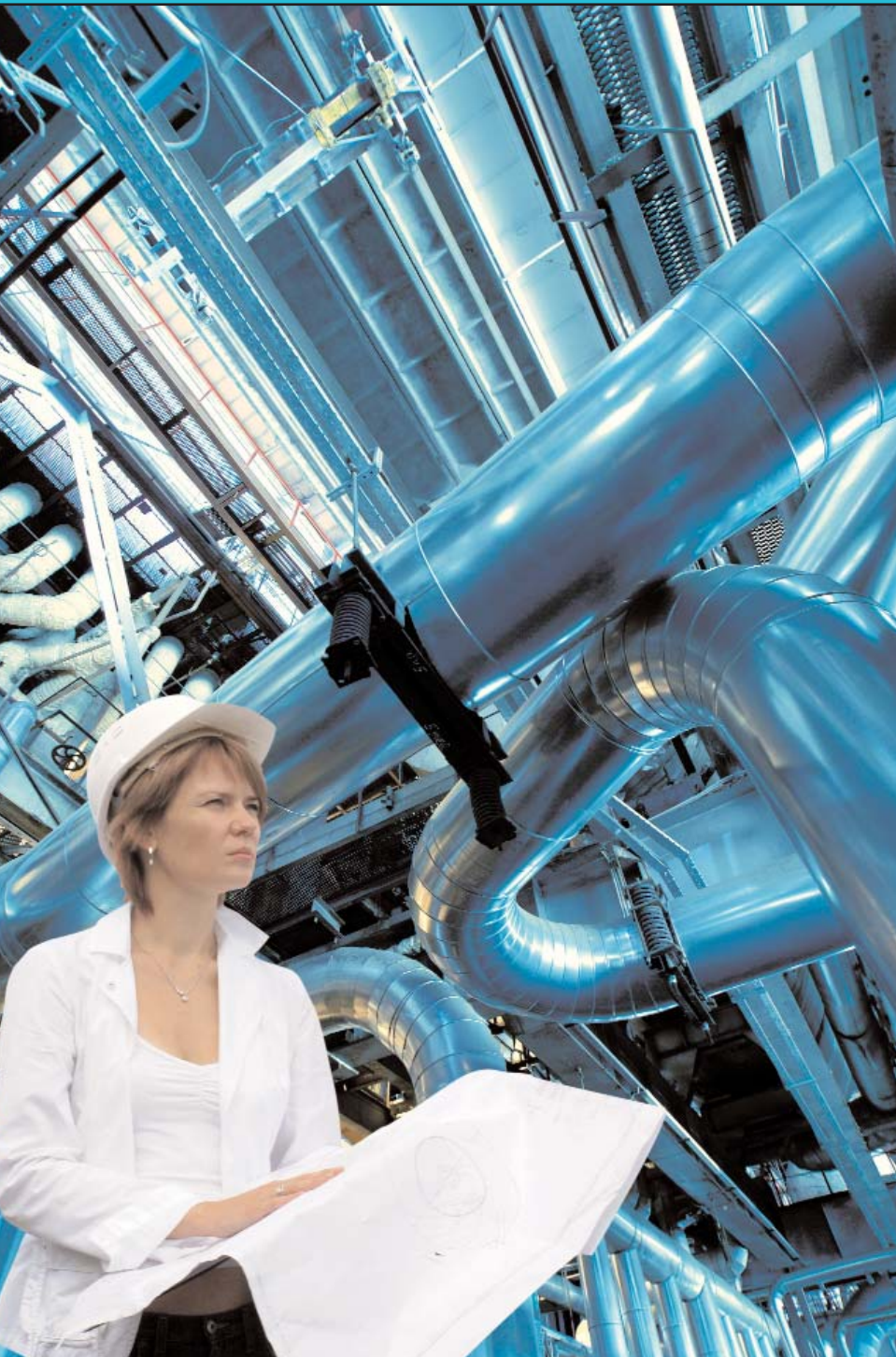


# Product Quality Research Institute (PQRI)

## Workshop on Sample Sizes for Decision Making in New Manufacturing Paradigms

September 12-13, 2011 in Bethesda



Co-sponsored by



in cooperation with  
ASTM Committee E11  
on Quality and Statistics



# Workshop

## PQRI

The Product Quality Research Institute (PQRI) is a non-profit consortium of organizations working together to generate and share timely, relevant, and impactful information that advances drug product quality and development. By virtue of its diverse membership, PQRI provides a unique forum to focus critical thinking, conduct research, exchange information, and propose methodology or guidance to pharmaceutical companies, regulators, and standard setting organizations.

## Scope and Objectives for the Workshop

The ability of pharmaceutical manufacturers to deliver quality product to the market place has become increasingly important. Technological advancements have made it possible to collect significantly larger amounts of data, but it is not always clear how to convert this data into statistically relevant information to enable decision making throughout the lifecycle of the product. The purpose of this workshop is to:

1. Clarify the roles and expectations of USP/EP and Regulatory Agencies with respect to statistical differences between acceptance criteria and process controls;
2. share approaches used to date to deal with large sample sizes;
3. discuss how information gained from larger sample sizes can be used to make better decisions during development and release of pharmaceutical products; and,
4. identify technical gaps or other challenges that prevent further progress for routine implementation.

While clearly a portion of this workshop will deal with statistical approaches, the material is intended to be understood by non-statistical workshop participants.

## Assumptions

- That CQA's are identified, that is, this workshop will not delve into how to determine what a CQA is.
- That quality data is being obtained from sensors, that is, the workshop will not go into details of how to utilize sensors in order to obtain quality data.

## Planning Committee

Sonja S. Sekulic, Ph.D., Pfizer Inc., **Chair**

Karthik B. Iyer, U.S. Food and Drug Administration, **Co-Chair**

Fernando J. Muzzio, Ph.D., Rutgers University, **Co-Chair**

Jim Bergum, Bristol Myers Squibb

James Evans, Ph.D., Massachusetts Institute of Technology

Sau (Larry) Lee, U.S. Food and Drug Administration

Christine Moore, Pharm.D., U.S. Food and Drug Administration

John J. Peterson, Ph.D., GlaxoSmithKline

Zhigang Sun, Ph.D., U.S. Food and Drug Administration

Gert Thurau, Ph.D., Merck & Co., Inc.

Yi Tsong, Ph.D., U.S. Food and Drug Administration

Alex M. Viehmann, U.S. Food and Drug Administration

## Monday, September 12, 2011

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**8:30 am**

### Workshop Introduction

Sonja S. Sekulic, Ph.D., Pfizer, Inc.

Karthik B. Iyer, Ph.D., U.S. Food and Drug Administration

Fernando J. Muzzio, Ph.D., Rutgers University

**8:45 am**

Moderator:

Sonja S. Sekulic, Ph.D., Pfizer, Inc.

**8:45 pm**

### FDA Perspectives on Larger Sample Sizes—Role of Regulators vs USP vs ASTM

Keith Webber, Invited

U.S. Food and Drug Administration

**9:15 am**

### The European Approach on Large Sample Sizes in the Context of a PAT Environment

Michael Wierer, Ph.D.

EDQM/Council of Europe

**9:45 am**

### The Role of USP

Anthony DeStefano, Ph.D.

U.S. Pharmacopeia

**10:15 am - 10:30 am**

### Coffee Break

**10:30 am**

### Designing and Optimizing Sample Plans

Swee-Teng Chin, Ph.D.

Dow Chemical Company

**11:15 am**

### Underlying Quality Considerations

Terrence Tougas, Ph.D.

Boehringer Ingelheim Pharmaceuticals

**12:00 am**

### Lunch

**1:00 pm**

Moderator:

John J. Peterson, Ph.D., GlaxoSmithKline

**1:00 pm**

### PTIT Approach: Developing Tolerance Interval Approach for Quality Assessment with Large Sample Sizes

Yi Tsong, Ph.D.

U.S. Food and Drug Administration

# Workshop

**1:30 pm**

**Content Uniformity Acceptance Testing for Large Sample Sizes: Nonparametric Counting Test**

Kim Vukovinsky  
Pfizer Inc.

**2:00 pm**

**The European Pharmacopeia Draft on Large Sample Sizes**

Oyvind Holte, Ph.D.  
Norwegian Medicines Agency

**2:30 pm**

**Demonstrating Capability to Comply with a Test Procedure: The Content Uniformity and Dissolution Acceptance Limits (CuDAL) Approach**

Jim Bergum  
Bristol Myers Squibb

**3:00 pm - 3:15 pm**

**Coffee Break**

**Breakout sessions**

**3:15 pm - 4:00 pm**

*Breakout Sessions will be repeated twice so all participants may attend both sessions.*

**Breakout 1: How Should We Be Testing for Pharmaceutical Process Control and Batch Release?**

Moderators:  
Karthik B. Iyer, Ph.D., U.S. Food and Drug Administration  
Kim Vukovinsky, Pfizer Inc.

**Breakout 2: What are the Regulatory Risks and Benefits of Smaller vs. Larger Sample Size Acceptance Criteria?**

Moderators:  
Lori Pfahler, Ph.D., Merck & Co., Inc.  
Sau (Larry) Lee, U.S. Food and Drug Administration

**4:00 pm - 4:45 pm**

**Breakout 1: How Should We Be Testing for Pharmaceutical Process Control and Batch Release?**

Moderators:  
Karthik B. Iyer, Ph.D., U.S. Food and Drug Administration  
Kim Vukovinsky, Pfizer Inc.

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Moderators:  
Lori Pfahler, Ph.D., Merck & Co., Inc.  
Sau (Larry) Lee, U.S. Food and Drug Administration

**4:45 pm - 5:30 pm**

**Day 1 Panel Question and Answer Session**

**6:00 pm - 7:30 pm**

**Networking Reception**

**Tuesday, September 13, 2011**

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**8:00 am**

Moderator:  
Karthik B. Iyer, Ph.D., U.S. Food and Drug Administration

**8:00 am**

**Focus Area: Blend Uniformity**

Fernando J. Muzzio, Ph.D.  
Rutgers University

**8:45 am**

**Focus Area: Content Uniformity—Current Landscape**

Steve Hammond  
Pfizer Inc.

**9:30 am - 10:00 am**

**Coffee Break**

**10:00 am**

**In-Process Particle Characterization—Regulatory Perspective**

Zhigang Sun, Ph.D.  
U.S. Food and Drug Administration

**10:30 am**

**In-Process Particle Characterization—Industry Perspective**

Martin Warman  
Vertex Pharmaceuticals, Inc.

**11:00 am**

**Merck Case Study: Half a Decade of Real-Time Release Testing on a High Volume Product**

Gert Thurau, Ph.D.  
Merck & Co., Inc.

**12:00 pm - 1:00 pm**

**Lunch**

**1:00 pm**

**Moderator**

Fernando J. Muzzio, Ph.D., Rutgers University

**1:00 pm**

**Process Validation Guidance—What Does 'Statistical Confidence' Mean?**

Francis Godwin  
U.S. Food and Drug Administration

**1:30 pm**

**Challenges of Statistical Analysis/Control in a Continuous Process**

James Evans, Ph.D.  
Massachusetts Institute of Technology

# Workshop

**2:00 pm**

## **Continuous Manufacturing—FDA Perspective on Submissions and Implementations**

Christine Moore, Pharm. D.  
U.S. Food and Drug Administration

**2:30 pm - 2:45 pm**

## **Coffee Break**

## **Breakout Sessions**

**2:45 pm - 3:30 pm**

*Breakout Sessions will be repeated twice so all participants may attend both sessions.*

### **Breakout Session #3: How Do We Integrate a Large Sample Size Approach into Pharmaceutical Quality Systems?**

Moderators:

Fernando J. Muzzio, Ph.D., Rutgers University  
Zhigang Sun, Ph.D., U.S. Food and Drug Administration

### **Breakout Session # 4: Are Pharmaceutical Companies and Regulatory Agencies Prepared for a Lifecycle Approach to Product Quality?**

Moderators:

Christine Moore, Pharm.D., U.S. Food and Drug Administration  
Gert Thurau, Ph.D., Merck & Co., Inc.

**3:30 pm - 4:15 pm**

### **Breakout Session #3: How Do We Integrate a Large Sample Size Approach into Pharmaceutical Quality Systems?**

Moderators:

Fernando J. Muzzio, Ph.D., Rutgers University  
Zhigang Sun, Ph.D., U.S. Food and Drug Administration

### **Breakout Session # 4: Are Pharmaceutical Companies and Regulatory Agencies Prepared for a Lifecycle Approach to Product Quality?**

Moderators:

Christine Moore, Pharm.D., U.S. Food and Drug Administration  
Gert Thurau, Ph.D., Merck & Co., Inc.

**4:15 pm**

## **Breakout Reports**

Day 1 - BO Session 1  
Day 1 - BO Session 2  
Day 2 - BO Session 3  
Day 2 - BO Session 4

**5:00 pm**

## **General Question and Answer Session**

**5:30 pm**

## **Closing Remarks**

Sonja S. Sekulic, Ph.D., Pfizer, Inc.  
Karthik B. Iyer, Ph.D., U.S. Food and Drug Administration  
Fernando J. Muzzio, Ph.D., Rutgers University

## **PQRI Mission Statement**

The Product Quality Research Institute (PQRI) is a non-profit consortium of organizations working together to generate and share timely, relevant, and impactful information that advances drug product quality and development.

By virtue of its diverse membership, PQRI provides a unique forum to focus critical thinking, conduct research, exchange information, and propose methodology or guidance to pharmaceutical companies, regulators, and standard setting organizations.

## **PQRI Member Organizations**

### **AAPS**

American Association of Pharmaceutical Scientists

### **CHPA**

Consumer Healthcare Products Association

### **FDA/CDER**

U.S. Food and Drug Administration, Center for Drug Evaluation and Research

### **HC**

Health Canada

### **IPAC-RS**

International Pharmaceutical Aerosol Consortium on Regulation & Science

### **IPEC-Americas**

International Pharmaceutical Excipients Council of the Americas

### **USP**

United States Pharmacopeia

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Glenn Van Buskirk, Ph.D., **Treasurer**  
Anthony DeStefano, Ph.D.  
Avraham Yacobi, Ph.D.  
Rachael Roehrig, Ph.D.

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*(REPRESENTATIVE AND ALTERNATES)*

Anthony DeStefano, Ph.D., **Chair**

### **AAPS**

Lynn Van Campen, Ph.D., John Lisack, Jr., CAE, Stacey May, M.A.

### **CHPA**

Rachael Roehrig, Ph.D.

### **FDA**

Helen N. Winkle, Nakissa Sadrieh, Ph.D., Raj Uppoor, R.Ph., Ph.D.

### **HC**

Anita DiFranco

### **IPAC-RS**

Terrence Tougas, Ph.D., Mary Devlin Capizzi, Esq.

### **IPEC-Americas**

Dave Schoneker

### **USP**

Kevin Hool, Ph.D.

# Workshop

The workshop is being held at the Hyatt Regency Bethesda and reservations may be made by calling **1-888-421-1442** and referring to the PQRI Workshop on SAMPLE SIZES. Hotel reservations can also be made online at <https://resweb.passkey.com/go/PQRW>.

Registration for the workshop can be made by going to the Sign Me Up website at [www.signmeup.com/75951](http://www.signmeup.com/75951)

For additional information, please contact Vicki Penn at [Pennv@pqri.org](mailto:Pennv@pqri.org).

