PDA Scientific and Regulatory Affairs

Josh Eaton
Senior Project Manager
What we do...

IGs & Volunteers
Coordinate 24 IGs in North America
Conduct Surveys

Advisory Boards
Facilitate Meetings
Prepare Technical Report Ballots
Assist in Member Selection

PDA Journal of Pharmaceutical Science and Technology
Established in 1947
Peer-reviewed
Published Bimonthly
Circulation of Over 10,000
Member Benefit

Regulatory Activities
Prepare Regulatory Comments
Strategic Planning
Participate in Regulatory Authority Meetings
Participate in PDA/PICS, PDA/FDA & PDA/EMA Meetings

Technical Reports
Review Technical Reports
Administration and Editing Activities

PDA Workspace
Technical Report Team Collaboration Space
Advisory Board Balloting Document Management

TRI Course Material
Develop PDA-Owned Courses
Act as Course Instructors
Plan Research Activities

Strategic Planning & Implementation
AB Member Training
Technical Report Team Training

Technical Report Dashboard
Over 50 TRs in Pipeline
Facilitate Technical Report Team (TRT) Meetings

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Industry interaction

- Regulatory commenting
- Points to Consider
- Surveys
- Research projects
- Technical Reports

Technical Report No. XX
Implementation of Quality Risk Management for Pharmaceutical and Biotechnology Manufacturing Operations

Paradigm Change in
Regulatory Commenting

PDA Members collaborate

Work to influence regulations based on scientific topics

Provide interpretation of quality and regulatory issues affecting development, manufacturing, and control of health care products
Recent commenting activity

**U.S. FDA**
- Contract Manufacturing Arrangements for Drugs: Quality Agreements
- Current Good Manufacturing Practice Requirements for Combination Products

**European Medicines Agency (EMA)**
- Guideline on Good Distribution Practice of Medicinal Products for Human Use
- Guideline on Similar Biological Medicinal Products

**China Food and Drug Administration (CFDA)**
- Draft Guideline on Process Validation

**Health Canada**
- Quality Draft Guidance Document: New Drug Submissions (NDSs) and Abbreviated New Drug Submissions (ANDSs)
Points to Consider publications

<table>
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<th>Reflective pieces upon industry</th>
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Topics addressed

| Pharmaceuticals | Biologics | Device manufacturing | Quality |

Represents global perspectives

| PDA individual member scientists and experts | Consolidated opinions and recommendations |
Aseptic Processing Points to Consider

Provides positions on current topics, best practices, and areas of clarification important to manufacturing quality sterile products

Guiding principles for developing the PtC:

1. Science and risk-based approach to manufacturing processes and control

2. Reduce risk to product quality through use of newer technology when feasible

3. Re-evaluation of traditional testing and monitoring methods

4. Thorough process and technical understanding of new product/container presentations, therapies, and technologies

5. Harmonization of global health authority requirements and guidance

Update of 2003 PtC
# Aseptic Processing Points to Consider

**Part 1**

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<th>Physical environment</th>
<th>Environmental monitoring</th>
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<td>Material transfer</td>
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<td>Filter integrity testing</td>
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**Part 2**

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<th>Focus</th>
<th>Aseptic process simulation/validation</th>
<th>‘Modern’ blow fill seal technology</th>
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<td>Critical utilities</td>
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Cleaning, disinfection, and sterilization

*Update of 2003 PtC*
Quality Metrics Points to Consider

Supportive of FDA quality metrics effort related to the Food and Drug Administration Safety and Innovation Act (FDASIA)

- Allows for metrics data to supplement or replace inspections
- Promotes continuous improvement

Based upon output of Quality Metrics conference co-chaired by FDA

- Need to move toward leading indicators to improve operations
- Includes definitions for recommended metrics
Surveys

Tools to determine state of the industry or technology

Gather data to support other technical efforts or to inform the Pharma community

Recent topics:

- Objectionable Microorganisms
- Process Validation
- Glass Quality
Objectionable Microorganisms Survey

**Purpose**

- Evaluate how companies and industries are handling the issue in non-sterile finished product formulations
- Output from survey also incorporated within the Technical Report
Objectionable Microorganisms Survey

Which item(s) are tested specifically for the presence of potential objectionable microorganisms?

- Environmental monitoring: 58%
- Utilities: 53%
- Raw Materials: 80%
- Packaging components: 21%
- Other: 4%
## Process Validation Survey

### Purpose

- Provide feedback regarding current industry status and practices related to the 2011 FDA Process Validation Guide
- To gain insight on challenges faced related to PV guidance
- Gauge how companies are implementing the new lifecycle approach to process validation
How is process validation defined in the quality standards/policies of your company?

- Three stages of process validation (Process Design, PPQ, CPV) - 30%
- One stage (Process Validation) - 63%
- Other (please specify) - 7%
# Glass Quality Survey

**Purpose**

- Determine what preventive measures needed to be considered by manufacturers, regulators and suppliers
- Better understand the cause/effect of these issues

In response to increased glass issues related to defects and/or incompatibilities with finished product over the shelf life.
Glass Quality Survey

How would you rate the overall glass container quality supplied by your suppliers?

- Exceptional: 51%
- Good: 41%
- Fair: 4%
- Poor: 4%
- Unacceptable: 0%
Research Projects

Environmental Monitoring technology comparison

- Began as an industry request
- Comparison of 1 specific technology versus a conventional EM technology
  - Laser-induced Fluorescence (LIF) vs. slit-to-agar sampler
EM technology comparison

Conducted in PDA’s manufacturing environment space

Data measurement:

• Total of 9 fills in Grade A space
• Total of 4 gowning processes in Grade B space
• 3 different LIF instruments were rotated through the spaces for each set of fill/gowning
• Utilized traditional particle monitors as event reference data
EM technology comparison

Results:

- All 3 LIF machines were capable of detecting fluorescent events which correlated positively with the slit-to-agar data
- LIF data provided was count/no count per 1 minute period
  - Recorded viable events only and non-viable data from LIF instruments was not considered for this study
- Number of events unavailable for slit-to-agar data comparison

Preliminary conclusions:

- Technology would work well for early warning of particulate level excursions
- Classification of events and identification of organisms still considered important
Technical Reports

What is a technical report?

Guidance and opinions written by subject matter experts

Address a wide array of challenging technical areas

Peer-reviewed global consensus documents

Used as references by industry and regulatory authorities
Technical Reports

*Nearly 80 technical reports produced*

- Multiple disciplines addressed

- Quality Risk Management
- Manufacturing Science
- Sterilization
- Microbiology
- Validation & Analytical Methods
Technical Reports

Technical Report No. 55
Detection and Mitigation of 2,4,6-Tribromoanisole and 2,4,6-Trichloroanisole Taints and Odors in the Pharmaceutical and Consumer Healthcare Industries

- Consumer complaints regarding tainted materials
- No safety risk found
- Smell was nausea-inducing

TBA and TCA cause moldy odors within package contents

Halophenols
- Low volatility
- Slight odor

TBA

TCP

TBP

Xerophilic fungi
25-35 °C
13-22% moisture

Haloanisoles
- High volatility
- Strong odor

TBA

TCA

OCH₃

Cl

Cl

Br

Br

OH

Br

Br

Cl

OCH₃

Br

Br

Cl
In 2010 and 2011, several pharmaceutical and consumer healthcare companies experienced issues with TBA taints.

- The TBA taints were evident in plastic packaging components and believed to be due to biomethylation of TBP, used as a preservative for lumber and to construct wood pallets.
TR 55: Detection and Mitigation of 2,4,6-Tribromoanisole and 2,4,6-Trichloroanisole Taints and Odors

PDA Task force was quickly formed

- Intensive research on cause/source of the TBA/TCA contamination
- Source confirmed as pallet materials

Technical Report produced as guidance for management of the issue

- Analytical methods
- Product quality monitoring
- Toxicology and safety
- Supplier/supply chain evaluation
TR 67: Exclusion of Objectionable Microorganisms from Nonsterile Pharmaceuticals, Medical Devices, and Cosmetics

TR Purpose

• Present strategies for managing microbial risks associated with the presence of objectionable microorganisms in nonsterile products
  – Covers nonsterile pharmaceutical drug products, over-the-counter (OTC) drug products, medical devices, cosmetics, and personal care products
CHALLENGE

How to define, monitor, and manage microbial risk?

Exclusion of objectionable microorganisms can an undefined critical quality attribute
TR 67: Exclusion of Objectionable Microorganisms from Nonsterile Pharmaceuticals, Medical Devices, and Cosmetics

Objectable Organism Decision Tree

Definitions

Growth in Product
1. Water Activity
2. Antimicrobial effectiveness test
3. Challenge

Organisms of Concern
1. Associated with outbreaks
2. Produces toxins
3. Clinically significant infections

Microbiology

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**Get involved!**

- Join an Interest Group
- Contribute to a regulatory comment submission
- Become a PtC or technical report team member
- Participate in a survey
- Propose your own idea
Questions?

Contact:

Josh Eaton

Sr. Project Manager, Scientific and Regulatory Affairs

Parenteral Drug Association® (PDA)

Bethesda Towers, Suite 150

4350 East-West Highway

Bethesda, MD 20814 USA

Tel: +1 (301) 656-5900, ext. 112

E-mail: eaton@pda.org