ISPE OSD Baseline Guide

• Professional guidance to global pharmaceutical industry that provides acceptable practice guidance tool in design and developing OSD facilities
• Provides a good guidance as starting point for industry professionals
• Delivers an acceptable practice for achieving regulatory compliance
Benefit from the ISPE OSD Baseline Guide

Intended to be used by various industry professionals for:

- Business Development
- Manufacturing Ops & Quality Management
- Regulatory Agencies, Inspectors & Auditors
- Science, Technology, Arch & Engineering
- Warehousing/Distribution

---|---|---

Volume 3 Rewrite - Team

 Approximately 75 Professionals

Lead by Steering Committee

Organized by Chapter

Overall ISPE Guidance

Chair and Co-Chair

Chapter Authors 2-10 people

Reviewers 10-15 people
Volume 3 Rewrite - Team

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ISPE Tech Writer

3rd Edition Progressive Outlines

Update Proposal & Initial Plan
June 2013

Team finalization, agreement and Rewrites
Nov 2013 - July 2014

Final Edits/GDC Reviews
4Q2015 (progress)

Officially Kicked off
Nov 2013

Annual Meeting

Industry Review and Revisions
Aug 2014 - Jan 2015

Industry Available Release
1Q2016
Numerous updates and considerations relating to modern OSD facilities in the areas of architectural (layout, functional areas, etc.), process support utilities (approach, critical systems, and code issues), HVAC (further aligned with the ISPE HVAC Good Practice Guide), electrical (classified areas, systems and preventive maintenance), controls and instrumentation (PAT, MES, EBR) and other considerations (non-cGMP risks, exposure, life/safety, hazardous operations, environmental, emergency preparedness).

Significant expansion of Product and Processing including the addition of ATEX, a European directive focused on equipment intended for use in potentially explosive situations.

- Revised the structure for better flow and communication
- Increased coverage of process technologies
- Risk Based Approach
- Incorporate with EU and JP standards and regulations, e.g. ATEX
- Quality by Design (QdB)
- Product Quality Lifecycle Implementation (PQLI)
OSD BG3 - Highlights

- Expanded discussion related to Risk Management (Chapter 3) with content including the topics of: Principles, Processes and Applicable Tools.
- Significant expansion of Product and Processing (Chapter 4) including the addition of “ATmospheric EXplosible (ATEX)”, a European directive focused on equipment intended for use in potentially explosive situations.

- New chapter entitled **Product Isolation and containment - Principles of Product, Operator, and environmental Protection.**
  - Detail on the challenges, and considerations relating to containment and cross contamination issues in OSD manufacturers

Quality by Design (QdB)

Aligned with ICH regulatory guideline Q8R2 as:

*A systematic approach to development that begins with predefined objectives and emphasizes product and process understanding and process control, based on sound science and quality risk management*
Key to Success
Process and Process Development

Protection by Design: Product, Process, Personal and Environment

Facility Layout, Critical Utility Criteria and Facility Equipment Configuration

Fit-in-use; Time-valued-Investment; Technological-Advancement

Facility Layout Comparison

Conceptual Future
Continuous Manufacturing with Robotic Warehouse
Benefits

Create more capable and capabilities in the global marketplace:

– Introduction of facility models which are:
  – smaller
  – more energy efficient
  – less wasteful
  – Opportunities for increasing productive
  – significantly less costly to build and operate
  – reduced WIP (Work In Progress) space and material

– Improves the quality control for consistency

– Decrease scale up issues and tech-transfer cycle time

Enable for faster launching of new products

Opportunity for reduction of Full-Time-Equivalents and increasing of OEE
PAT and CMP

The way of our future
Pharmaceutical Manufacturing Operations

High inventory including “work in progress”, long changeovers, disconnected processes, high process losses, off line analysis, low asset utilization, …
Granulation Processes Review

DIRECT COMPRESSION

Designs compatible with Continuous Operations

DRY GRANULATION

Batch by Nature

WET GRANULATION

Continuous Processing

In- Line Granulation

IN-LINE HIGH SHEAR GRANULATOR
Continuous Processing
Fluid Bed Dryer Concepts

What to Understand: Product CQA and Process Control Requirements

Critical-to-Quality Attributes (CQA)
What to Control: PAT Quality Data Management System

Blender
Granulator
Dryer
Quality check
Tablet press
Coating

PAT?

\[ (x + a)^n = \sum_{k=0}^{n} \binom{n}{k} x^k a^{n-k} \]
PAT in Solid Dosage

• Drying control
• Process parameters
• Loss On Drying
• Content Uniformity
• Bulk Physical Defects

• Wet Granulation
• Process parameters
• Liquid addition
• Blending / Lubrication control
• Process parameters
• Particle size
• Sampling & Off-line analysis

• Compression control
• Process parameters
• Coating solution
• Coating thickness

• Coating control
• Process parameters
• Packaging

• Dispense & Blend control
• Process parameters
• Liquid addition
• Api & Excipients

• Input material characteristics
• Process parameters

• Assay
• Dissolution/disintegration (NIR)
• Visual Inspection
• Coating thickness

• Particle size (Malvern)
• Weight
• Hardness
• Thickness

• Particle size
• Sampling & Off-line analysis
• Test against specifications
CQA to CPP – the Specification

Efficiency

• Processes will require less Foot-Prints, less Initial-Capital
• Operation could be continuous for 24/7
  – Fewer startup/shutdown quality problems
  – 100% capacity utilization (OEE)
• Closed Operation with Fully Automated Systems
  – Less Human Intervention; Less operator exposure to product
  – Less Exposure to Environment; Less Exposure of Cross-Contamination to Product
• Just-in-time operation minimizes the product storage and in-process quarantine
Statistical Data Suggests

- **Continuous Manufacturing** must be aligned with **PAT**
  - Reduced scrap/rework
  - Reduced human errors
  - Increased & consistent product quality
  - Reduced quality costs
  - Reduced regulatory compliance costs
  - Faster time to market: scale-up & tech transfer
  - Real-time product release

- **The future is not a million miles away; it is here, in Boston Area!**