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ASTM E2500 and FDA's (draft) Process Validation Guidance

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Agenda

- Background of consensus standards and ASTM E2500
- New FDA validation guidance
- ASTM Standard Content
- ASTM vs. FDA guidance

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Consensus Standards - General

- Consensus standards bodies
- Consensus process
- Participation in consensus standard development
- Traceable to World Trade Organization

(OMB) Circular A-119

- The law requires use of voluntary standards except "when it is inconsistent with the applicable law or otherwise impractical."

ASTM E2500

Standard Guide for Specification, Design, and Verification of Pharmaceutical and Biopharmaceutical Manufacturing Systems and Equipment

ASTM E2500 Current Situation

- Standard approved August 2007
- Many companies studying implementation
- Some projects partially or fully implementing
- ISPE Baseline guide Volume 12
- ISPE Good Practice Guide

New FDA Guidance Document

- Update to 1987 Process Validation Guide
- Issued for comment 11/18/08
- Focuses on process validation
- 1 page devoted to equipment qualification
- ISPE and others have commented to FDA

Three Phases

- Process design
- Process confirmation (process qualification)
- Process monitoring (continued process verification)

Phase II: Process Confirmation

- Equipment suitability (Equipment qualification)
- Conformance lots (performance qualification)

Equipment qualification

- Umbrella term for activities undertaken to demonstrate suitability for intended use
- Specifics (IQ, OQ, protocols) not defined
- Risk management to prioritize
- QA unit approve plan and report

Performance Qualification

- Prior to commercial distribution
- No minimum number of lots
- Use of statistical techniques
- Protocol - execution - report

FDA Draft: The Good

- Understand the product and process
- Design an efficient process
- Design facilities, utilities and equipment for their intended use
- Commission to demonstrate suitability for use
- Qualification is umbrella term for many activities

FDA Draft: Specifics

- Select utilities and equipment appropriate for their specific use
  - Materials of construction
  - Operating principles
  - Performance characteristics
- Verify they will meet process requirements in all anticipated operating ranges

FDA Draft: Key Points

- Consider requirements of use
- Incorporate risk management
  - Prioritize activities
  - Identify level of effort (activity performance and activity documentation)

FDA Draft: The Questionable

- Excludes automated systems
- Overly prescriptive on details of testing
- Overly prescriptive on details of QA role
  - Beyond that required by GMP regulations

ASTM E2500

Content Review

Scope of Standard

- Pharmaceutical and Biopharmaceutical
  - Systems and process equipment
  - Supporting utilities
  - Equipment automation and process control
- Laboratory systems and equipment
- Information systems
- New facilities
  - Changes to existing (may be used)

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Key Concept/ Principle #1

Risk-Based Approach

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Key Concept/ Principle #2

Science-Based Approach

Key Concept/ Principle #3

Critical Aspects

Key Concept/ Principle #4

Quality by Design

Key Concept/ Principle #5

Good Engineering Practices

Key Concept/ Principle #6

Subject Matter Experts

Key Concept/ Principle #7

Use of Vendor Documentation

ASTM Process

- Requirements Definition
- Specification and Design
- Verification
- Acceptance and Release

Supporting Activities

- Good Engineering Practice
- Risk Management
- Design Review
- Change Management

Process

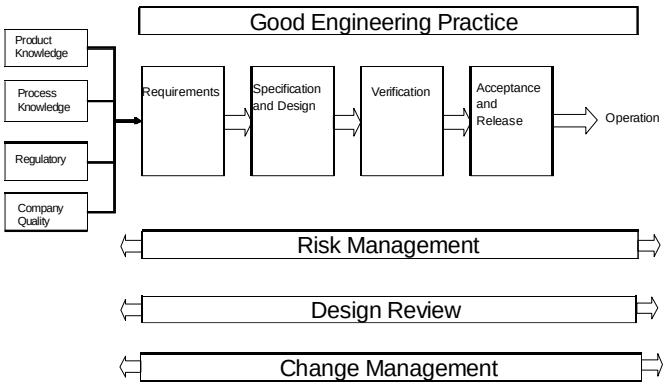

Figure 1 Š The Specification, Design, and Verification Process

Requirements

- Product and process knowledge
- ICH Q8 Design Space
- Specific requirements based on:
  - Product knowledge
  - Process knowledge
  - Regulatory requirements
  - Company quality requirements

Specification and Design

- Companies determine how to:
  - Communicate requirements
  - Embody requirements in equipment and system design
  - Focus on those aspects critical to product quality and patient safety
  - Critical elements should be identified and documented by subject matter experts

Verification

- Systematic approach, documented
- Extent of verification activities: based on risk
- Acceptance criteria
- Verification plan
- Verification activities
- Verification review

Acceptance and Release

- Departures from specification
  - Role of subject matter experts
  - Role of quality unit
- Acceptance and release review/ report
  - Role of subject matter experts
  - Role of quality unit

Supporting processes

- Risk management
- Design Review
- Change management

Documentation

- Subject matter experts (per 21CFR 211.25)
- Determine how to inspect, test and adjudicate results
- Quality unit approve verification plan and report if system contains critical aspects
- Risk to patient considered in level of effort, formality, documentation

Summary

Qualification/ verification aspects	FDA	ASTM
Focus on science-based process understanding and meeting process requirements	X	X
Equipment and facilities suitable for intended use	X	X
QA approves [qualification] [verification] plan	X	X
QA approves [qualification] [verification] report	X	X
Risk assessment to “scale” effort, documentation	X	X
Flexibility on how effort is structured	X	X

Summary

Qualification/ verification aspects	FDA	ASTM
Specific aspects to check spelled out	X	
Critical aspects defined from risk assessments and process requirements		X
Use of project change management	X	X
Use of subject matter experts: how to verify, adjudicate minor departures from specification		X
Use of vendor documents		X
Design of facility, process, equipment based on process understanding	X	X

Questions?

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