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

Robert E. Chew, PE
President
Commissioning Agents, Inc.

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Agenda

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


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)

Key Concept/ Principle #1
Risk-Based Approach
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

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

Figure 1: 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

<table>
<thead>
<tr>
<th>Qualification/ verification aspects</th>
<th>FDA</th>
<th>ASTM</th>
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<tbody>
<tr>
<td>Focus on science-based process understanding and meeting process requirements</td>
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<td>X</td>
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<tr>
<td>Equipment and facilities suitable for intended use</td>
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<td>QA approves [qualification] [verification] plan</td>
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<td>QA approves [qualification] [verification] report</td>
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<tr>
<td>Risk assessment to “scale” effort, documentation</td>
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<td>Flexibility on how effort is structured</td>
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<td>Specific aspects to check spelled out</td>
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<td>Critical aspects defined from risk assessments and process requirements</td>
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<td>Use of project change management</td>
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<td>Use of subject matter experts: how to verify, adjudicate minor departures from specification</td>
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<td>Use of vendor documents</td>
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<tr>
<td>Design of facility, process, equipment based on process understanding</td>
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Questions?

Robert E. Chew, PE
+1 317 710 1530
Robert.Chew@Cagents.com