Quality By Design (QbD) Verses Validation

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What is QbD?

- Design according to current industry standards
- Good Engineering Practice (GEP)
- A FULL understanding of the product attributes as related to product performance

- Deals with assessing and mitigating Risk

What is Validation?

Approach

Stages of C & Q

- Design Review
  - Change Control
- FAT vs. SAT
- Commissioning
- Verification
- Validation

Old Way

- Design
  - Design Review
- Construction
  - Construction Review
- Utilities Installed
  - IQ
- Equipment Installed
  - IQ

Current

- Current C & Q activity is based on FDA "*Final Report Pharmaceutical CGMPs for the 21st Century*"
  - Adopt NEW technologies early
  - Facilitate application of Quality Management
  - Use Risk Based Approach
- Multi Country Acceptance
  - ICH Q8 and Q9

Old Way

- Utilities
  - OQ
- Equipment
  - OQ
  - PQ
- Process Validation

New Way

- Design
  - GEP
  - ASTM E2500
- Assess Risk(s)
- Commission
- Qualify
- Validate

Some Questions to Ask

- Is the step a CQA or CPP?
- How necessary is the step for product efficacy ?
- How complex is the equipment?
  - What can go wrong?
- What are the specifications for the equipment?
  - How critical are the specs?

Example 1

- Mixer
  - Blend uniformity is a CQA
    - Is it the only mixing step?
    - Where in the process is the mixer?
    - Is it mixing critical components?
  - Specifications for the mixer and the mixing
    - Blended uniformily

Example 2

- Granulator
  - Is particle size a CQA?
  - Specifications
    - Size uniformity
    - Temperature

Example 3

- Holding Tank
  - Is there a CQA involved in this step?
  - Specifications
    - Temperature
    - Mixing

RISK

RISK

- What is it?
- What Types of Risk Can We Expect?
- What Type of Risk Can We Accept?
- How Much Risk Can We Allow?

Types of Risk

- Machine
  - Failure (part or whole)
  - Internal vs. External
- Ingredients
  - APIs
  - Excipients
- People
  - Operators
  - Maintenance
  - Cleaning
- Training
  - Understanding
  - Commitment

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RISK

- IS
  - How **severe** on/for production
  - How **often** CAN it occur
  - How will it be **detected**
    - How often can it be detected
  - How will the **PATIENT** be affected
- IS NOT
  - The possibility of getting caught

Ignorance is Risk

The FDA and Others

ASTM E2500 - QbD

- Not an FDA document
- Objective
  - Provide manufacturing capability to support defined and controlled processes

FDA Approach to Risk

- PAT – Process Analytical Technology
- ICH Q9 – Risk Management
- QSIT – Quality Systems Inspections Technique

Science Based Approach

- Complete understanding of the Process
- Leverage scientific knowledge to support
  - Design
  - Development
  - Verification

Specifications

- Who develops the specs?
- What specs do you need?
  - User Specs
  - Design Specs
  - Vendor Specs
- How are they used?

Be Flexible

- Be creative in the use of IQ/OQ/PQ
- Use of EQ
- Decide the BEST approach based on the regulatory needs AND Patient safety
- Define your objectives carefully and clearly

Flexibility

- Base qualification protocols on the Risk
  - CQA or CPP involved
  - Product Completion
  - Replaceable parts/unit
- More is NOT Necessarily Better
- Less may earn a 483

Good Engineering Practice (GEP)

- Engineering practices that are applied throughout the business
- Provides
  - Organization
  - Control
  - Effective Solutions
- NOT A GxP function

SMEs

- What is an SME?
  - Have specific expertise in a particular area
- Who qualifies as an SME?
- Why use an SME?

Validation vs. Verification

- Validation is:
  - Documented evidence that the equipment or process will function as designed with a High degree of assurance
- Verification is:
  - Demonstrating that the equipment or process works as intended

SUMMARY

QbD v. Validation

- QbD
  - Consider Risk
  - Know the process
  - Use GOOD Science
- Validation
  - Consider Risk
  - Know the process
  - Use GOOD Science
  - Test – Test - Test

QbD v. Validation

- Validation STILL needs to be performed
- IQ and OQ can be ***minimized*** IF the RISK is LOW

- Now more than ever the process MUST be better understood and controlled

Thank You!

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