Validation Science and Practice

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Far Sight Skills Development

Overview

General Reminders

Technical and Regulatory Points to Consider

A Foray into Statistical Methods

Wrap Up and Questions

General Reminders

- Our focus today on FDA's 2011 Guidance Document – a "new" document
- The document itself reminds us of what regulators do (so well)
- The Guidance Document is not for medical devices and dietary supplements

(More) General Reminders

- In-process and final product checks offer limited assurance of quality
- The definition of validation has not changed
- The overarching claim remains the same

Technical / Regulatory

- Process Validation is aligned with the “life-cycle” of a process
- Quality / safety / efficacy to be built into the product by design
- The current focus is on variations, variations and variations

Technical / Regulatory

- Process Variations
  - where they come from
  - detecting and measuring them
  - knowing their impact
  - defining and implementing risk-based controls
- A remark concerning retrospective validation

Technical / Regulatory

- Process Validation takes place throughout the process life cycle

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  Stage 1 – Process Design

Technical / Regulatory

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  Stage 2(a) – facility design

Technical / Regulatory

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  Stage 2(b) – PPQ process performance qual

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  Stage 2(b) – PPQ process performance qual

  Stage 3 – Ongoing verification

Metrics and Measurement

Guidance on Process Performance Qualification is clear

- "*cumulative data* from all relevant studies"
- "firms to employ *statistical metrics*"
- "*performance indicators* that allow risk-based decision-making
- such decision-making to be based on "*statistical methods*"
- "*persons with adequate training in statistical process control*" are recommended

Still, industry interprets and regulators judge

Metrics and Measurement

- The Golden Rule of 3 PPQ batches no longer meets “c” GMP.
- Your approach to PPQ is based on residual risk – (not discussed today)

We will wander into the topic of statistical process control.

Fun Forays into Statistics

Process Capability and Process Capability Index (C_p) and (C_pK)

- **Well established concepts in six-sigma school of thought**
- **Can be calculated – functions of specification limits (for you to say) and process wobble (goodness of control)**
- **The expectation is that your process runs between 1.0 and 1.6**

Some perspective will be helpful

Fun Forays into Statistics

Frequentist (or classical) statistics

- **Remember mean and standard deviation are only estimates**
- **They are backward (or at best current) looking**
- **Limited assurance of future control hence not ideally suited for validation.**

Fun Forays into Statistics

Bayesian statistics

- **Meet Thomas Bayes**
- **Probability is expressed as a future likelihood**
- **We all operate this way and it's the basis for artificial intelligence**
- **Assurance (likelihood) of future control is based on an existing body of knowledge updated with new evidence.**

Summary Points

Validation Remains a Science / Discipline

The life-cycle approach leads to a better understanding of the process

An increasing level of rigor will be expected, but keep in mind the time constant for change

Develop your internal regulatory strategy