
Post-Approval Manufacturing Changes

Office of Compliance Perspective

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Oversight of Post-approval Changes

Synergy

CMC review
&
GMP program

CGMPs and the Desired State

A modern CGMP program includes two fundamentals:

- Science-based Change Control Procedures
- Sound Quality Risk Management

Types of Regulation

- Technology-Based
- Performance-Based
- Management-Based

Coglianese and Lazer (2003)
Law and Society Review

Types of Regulation

Technology-Based regulation:

Technology based approaches intervene in the acting [production] stage, specifying technologies to be used or steps to be followed to achieve a social goal.

Performance-Based regulation:

Performance-based approaches intervene at the output [testing] stage, specifying social outputs that must (or must not) be attained.

Types of Regulation

Management-Based regulation. Under this approach, firms are expected to:

- produce plans that comply with **general criteria** designed to promote the targeted social goal.
- **evaluate and refine management** systems with respect to the stated social objective.

Management-Based Regulation

- *Places responsibility for decision-making with those who possess the most information about risks and potential control methods*
- *Provides flexibility for firm to create their own regulatory approaches, enable firms to experiment and seek out better, more innovative solutions.*

Post-Approval Change Under a **Management-Based** Regulatory Strategy

- Regulatory hurdles lowered to facilitate the adoption of advances in manufacturing technology
- Integration of continual improvement into manufacturers' process control strategies
- Emphasizes a firm's ultimate responsibility for ensuring quality of their products
- Inspections monitor effectiveness of a firm's quality system in implementing changes

Guidance for Industry Quality Systems Approach to Pharmaceutical CGMP Regulations

<http://www.fda.gov/cder/guidance/7260fnl.htm>

ICH Q10

Quality Systems and Process Control

“A **quality systems approach** calls for the manufacturer to develop procedures that monitor, measure, and analyze the operations (including analytical methods and/or statistical techniques). **Monitoring of the process is important due to the limitations of testing.**”

Early Detection and Root Cause Correction

“If the underlying hazard is **quickly identified and remedied**, the likelihood of the event recurring is either greatly reduced or eliminated. If not identified, disclosed, and **properly managed**, the incident may be forgotten and the latent potential for damage remains.”

“Far reaching and more **permanent solutions rectify root causes**”

Process improvement is facilitated by: “a well-designed infrastructure for recognizing, reporting, analyzing, identifying, and **implementing solutions to prevent future**” problems.

Phimister, et al. (2003)
Journal of Risk Analysis,

Change Control Procedure

- Reliably estimates risk posed by a proposed change
 - determines potential for product impact/hazard
- Determines needed scrutiny for the change
- Documents the change and the results
- Evaluates the actual impact of the change

Summary

- Management-Based Regulation, coupled with regulatory guidance and inspectional oversight, provides the foundation for the “Desired State”
- Good manufacturing practice *and* good business practice are supported by a robust quality system. This includes:
 - Science-based change control procedures
 - Sound Quality Risk Management

References

Coglianesi and Lazer (2003). Management-Based Regulation: Prescribing Private Management to Achieve Public Goals, *Law and Society Review*, 37, 691-730.

Phimister, James, *et al.*(2003). Near-Miss Incident Management in the Chemical Process Industry, *Risk Analysis*, Vol. 23, No.3, 445-459.