Change Management

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OBJECTIVES

• Understand requirements for Change Management/Change Control

• Discuss common problems with Change Control Programs

• Regulatory Expectations for Change Control

• Best Practices for a Change Management Program
**DEFINITION**

Change...According the Merriam-Webster dictionary

1: to make or become different
2: to become something else
3: to undergo alteration or replacement
4: to vary

Synonyms: alter, make over, modify, recast, redo, refashion, remake, remodel, revamp, revise, rework, vary
DEFINITION

Change Control/Change Management: (Generally terms can be used interchangeably) - Source anonymous...

“A formal system by which qualified representatives of appropriate disciplines review proposed or actual changes that might affect a validated or controlled status. The intent is to determine the need for action that would assure and document that the system is maintained in a validated or controlled state”.
PURPOSES OF CHANGE CONTROL

• To prevent unwanted, unapproved, and unintentional changes to validated processes, procedures, methods, equipment, documents, and facilities

• To create a structured procedure to assure all changes are properly specified, designed, reviewed, assessed for risk, approved, and documented to assure changes will not adversely impact product quality, safety, identity, or purity of drug products

• To prevent unauthorized changes

• To assure changes are correctly implemented and compliant with GMP requirements
ICH Q10 - PHARMACEUTICAL QUALITY SYSTEM

Change Management is an integral part of the Pharmaceutical Quality System – which has been adopted by most regulatory agencies.

• “Change” is mentioned 27 times in ICH Q10

• ICH Q10 definition- Change Management:

  “A systematic approach to proposing, evaluating, approving, implementing and reviewing changes.”

Change Management System - excerpts from ICH Q10

• In order to properly evaluate, approve and implement changes, a company should have an effective change management system.

• The change management system ensures continual improvement is undertaken in a timely and effective manner while providing a high degree of assurance there are no unintended consequences of the change.
The change management system should include the following, as appropriate for the stage of the lifecycle:

1. Quality risk management (ICH Q9) should be utilized to evaluate proposed changes. There should be an assessment to determine whether a change to the regulatory filing is required under regional requirements.

2. All changes should be properly evaluated.

3. Proposed changes should be evaluated by expert teams contributing the appropriate expertise and knowledge from relevant areas, e.g., Pharmaceutical Development, Manufacturing, Quality, Regulatory Affairs and Medical, to ensure the change is technically justified. Prospective evaluation criteria for a proposed change should be set.
(4) After implementation, an evaluation of the change should be undertaken to confirm the change objectives were achieved and that there was no deleterious impact on product quality; (Effectiveness Check)

(5) Regulatory submission/approval requirements should be assessed for a proposed change to a marketed product.
Change Management and Product Lifecycle

• Change in Development: Change is an inherent part of the development process and should be documented; the formality of the change management process should increase as the product moves through development.

• Change in Technology Transfer: The change management system should provide management and documentation of adjustments made to the process during technology transfer activities.

• Change in Manufacturing: A formal change management system should be in place for commercial manufacturing. Oversight by the quality unit should provide assurance of appropriate science and risk based assessments.
COMMON CHANGE PROBLEMS

- Failure to follow the change management procedure
- Failure to adequately describe the change(s)
- Failure to adequately document the reason/rationale for change
- Failure to perform a complete, in-depth risk assessment
- Failure to provide complete documentation
  - Any reviewer/approver must have complete information upon which to base the approval – this includes such things as revised (marked-up) documents, new documents, P&IDs
- Failure to include users as part of the change process
COMMON CHANGE PROBLEMS

• Failure to obtain appropriate approvals before implementing a change
  • Unauthorized changes are often implemented in an effort to improve operations

• Failure to identify all tasks associated with the change, such as updating documentation, training, etc.

• Failure to confirm change is completed as approved, associated tasks are completed and to determine and document that the change achieved the intended purpose

• Lack of awareness training to all employees regarding changes

• Failure to provide a complete documentation package suitable for review and understanding by a third party
  • Documentation is necessary for proper internal review and approval, but the same documentation may be reviewed some time later by a third party (or regulator)
COMMON CHANGE PROBLEMS

• Most unauthorized changes are made with good intentions
  • Employees believe there is a better, more efficient way to do something
• The change control process is too cumbersome and employees work out ‘go-arounds’ or short-cuts
CHANGE CONTROL – WHY DO CHANGES NEED TO BE MANAGED?

Examples of changes made without proper assessment are numerous – Two classic examples:

• The “green batch”…..
  • Unauthorized change made to “improve the appearance of equipment”

• The loss of 19 batches due to failure of microbial limits test
  • Unauthorized change made to improve packaging line capacity
CHANGE CONTROL – WHY DO CHANGES NEED TO BE MANAGED?

API manufacturer

- Between 2nd and 3rd validation batches, manager decided to ‘improve’ the appearance of filter/dryer before PAI
- Production manager removed the agitation blade and had it ‘chromed’
- Unfortunately the API reacted with the ‘chrome’ and turned the white API green
- Result: Validation batch failed based on color
- All other specification elements passed and rejection reason was not process related
CHANGE CONTROL – WHY DO CHANGES NEED TO BE MANAGED?

Topical ointment manufacturer

- Products non-sterile but with microbiological limits
- Large production room with 2 packaging lines
- Area Manager decided to install a wall to divide room so 2 products could be produced at same time
- Work done on weekend with local funds
- Two weeks later micro failures show up
- Investigation: All air inlets on one side of wall, all exhaust on the other side – inadequate air circulation
- Result: Several days production rejected.
SOURCES OF CHANGES

• Planned improvements, scale-up and development

• Deviations/product failures/OOS results

• Annual Product Quality Reviews

• Internal/External Audits

• Complaints

• Customer requests

• Contractor requests

• Regulatory requirements or inspections
**SOURCES OF CHANGES**

- Many changes are made during the process of implementing new systems or corrective actions. The Change Control Quality System should be well-established.

- Change Control should be a top priority Quality System to any facility expansion or corrective action plan.
CHANGE CONTROL = COMMUNICATION
REGULATOR EXPECTATIONS

• Change Management is highly visible to regulators since it is a “non-routine” activity

• Change Control must include changes to:
  • Documents
  • Facilities
  • Utilities
  • Raw Materials/Suppliers
  • Production Processes and Equipment – including cleaning procedures
  • Computer Hardware/Software
  • QC/Analytical Methods, Specifications and Instrumentation
REGULATOR EXPECTATIONS

Expectations are that the change control system document . . .

- Description of the change – “from” – “to”
- Rationale for each change
- Risk/Impact assessment
- Review and approval of appropriate departments
- QA involvement/review
- Post-change effectiveness check
CHANGE CONTROL PROCEDURE (SOP)

• Ensure ALL changes are captured

• Suggest a single change control procedure –
  • Perhaps individual procedures for documents and computers are appropriate

• Single point of coordination – generally QA

• Judgment must be documented regarding effects/impact upon:
  • Product Quality
  • Regulatory Filings
  • Qualification
  • Validation
  • Stability

• Linkages to other Quality Systems – validation, QC, training, deviations
CHANGE CONTROL PROCEDURE (SOP)

• Should be “User Friendly”

• Provide a process for temporary changes

• Provide a process for emergency changes
  • Quality impact evaluation the next business day

• Address preventive maintenance and repairs

• Address “like-for like” part changes (not subject to change control)

• Instill the concept that all changes must be approved before implementation
WHO MUST BE TRAINED?

• All users of the change control system and forms must have formal documented training.

• All employees should receive basic change control ‘awareness’ training which includes:
  – Contractors such as cleaners in GMP areas
  – Temporary employees
  – Top management
APPROVALS

Who MUST approve changes?
• User Department
• Quality Assurance

Who SHOULD approve changes?
• Regulatory Affairs
• Additional Units:
  • Maintenance/Engineering
  • Material Control
  • Purchasing
  • Quality Control
  • IT
  • R&D
CHANGE CONTROL - GENERAL BASIC STEPS

• Origination and completion of Change Request
  • Anyone should be able to raise the issue that a change is necessary
  • Change Request should include:
    – Requesting department
    – Date change needs to be in place
    – Systems or process affected
    – Current practice or condition
    – Describe what will be changed – future state
    – Reason/rationale for change

• Initial department management review

• Route to QA for Identification & logging – determination of class of change, if required
CHANGE CONTROL - GENERAL BASIC STEPS

• QA determines proper reviewers

• Change documentation package is circulated to reviewers

• QA receives and consolidates comments

• Additional tasks are determined

• Final draft of change circulated for final approval

• Effectiveness check method is determined QA
CHANGE CONTROL - BASIC STEPS

• Conduct change-specific training

• Additional tasks accomplished

• Change is implemented

• Communicate the change

• Effectiveness check by QA to make certain change was implemented as approved and accomplished intended outcome.

• Change closure

• Retention of change documentation

• Periodic review and change trending
CHANGE TYPES

- Planned Changes
- Unplanned Changes
- “Planned Deviations”
- Temporary Changes
**CHANGE TYPES**

*Planned Changes*

- Permanent or temporary changes where the Change is approved prior to the change.

- Change is known in advance such that potential impact can be evaluated prior to the change being implemented.
Unplanned Changes

• Changes where the Change is not or cannot be evaluated and is NOT approved prior to the change.

• These are generally emergency changes, such as equipment repairs during production operations.

• Generally unplanned changes are actually deviations and should be handled and investigated as such.
**CHANGE TYPES**

**Planned Deviations**

- “Planned deviations” is a term often used (actually misused) – a terrible misnomer sometimes used for temporary changes

- No one should “plan to deviate”

- Deviations are **unplanned** events that must be investigated and impact must be evaluated after the event has occurred.

- Planned deviations are **actually changes** and there is an opportunity to evaluate the impact prior to the change implementation.

- The term should be removed from company vocabulary
**Temporary Changes**

- Changes for a specified limited duration where the change can be approved prior to the change being implemented with the intention of returning the system to its previous state.

- Temporary changes are for a certain time or for a specified number of batches.

- Evaluation of impact **must** be the same as for permanent changes since the change could have potential adverse impact even if only a single batch is produced under the temporary change conditions.
Changes with respect to CMOs and Suppliers:

Manufacturers are responsible for changes that are made by CMOs and material/packaging component suppliers. Provisions for changes should be detailed in the Technical/Quality Agreements which should include:

- Notification from CMO/supplier with appropriate documentation to enable assessment prior to change implementation
- Internal procedure for review, assessment, and approval of external changes.
- Determine follow-up actions such as use tests, stability, etc.
- Contractor must have own change control procedure
- Certain changes require applicant approval, others, only notification
SUMMARY

• Ensure Change Control Procedures are followed for all changes
• Ensure the reason/rationale for change is documented
• Ensure approvals are obtained before implementing changes;
• Communicate the change
• Conduct necessary training
• Evaluate change effectiveness following change implementation
• Ensure change documentation can be used to defend the release or rejection of a batch and can withstand review by third parties
THANK YOU!

QUESTIONS?