



Implementing the Requirements of the IPAC-RS Guideline

Case Study: Control Change

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Overview

- Introductory Thoughts
 - Source material for this presentation
 - Why is change control important to OINDP?
- What does the IPAC-RS GMP Guideline say about change control?
- Supplier Perspective on Change Control
 - Scope
 - Overview of a supplier change control process
 - Designing and implementing change control program

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Source of Presentation

- West Pharmaceutical Services revamped its change control program
- Although change was made prior to publication of IPAC-RS Guideline, new program is in line with principles expressed in guideline
- This presentation provides high-level overview of process

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Why is Change Control Important for OINDP Components? (Reminder from Morning Context Presentation)

- OINDP considered “highest risk” by FDA
 - Drug delivery via inhalation is as quick as an injection in many cases
 - For respiratory products, drug is being delivered directly to the diseased organ (lung)
 - Lung/respiratory system less robust than, *e.g.*, digestive system
- Each OINDP device is composed of multiple components from multiple materials
 - Components and their properties can significantly impact device performance and drug delivery
 - *E.g.*, rubber valve with improper additives may swell
 - Change in antioxidant package may impact component functionality
 - Change in cleaning process may result in new foreign particulates or leachables
 - Change to resin or a component of the resin may change the extractables/leachables profile



Consequences of Unapproved/Unanticipated Component or Material Change

- **Best Case:** unapproved changes to component/material is detected at receipt/ inspection/testing of incoming component/material by the customer.
 - Results in supplier investigation (time/resources); material return/scrap; customer production delays.
- **Worst Case:** unapproved changes to component/material causes final product failure in the field.
 - Customer (OINDP manufacturer) must recall product
 - **FDA Notification**
 - **Cost**
 - **Customer market perception**
 - Time must be spent on investigations to determine and fix root cause of problem

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Therefore:

- Changes should be adequately controlled through a change control process
 - OINDP manufacturers and suppliers should discuss, understand, and agree on:
 - What constitutes a significant change
 - What type of changes require notification and/or approval
- à This presentation focuses on the change control process and what it includes

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What Does the IPAC-RS Guideline say about Change Control?

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IPAC-RS Guideline on Change Control: 9 Points

- 1) OINDP suppliers shall establish and maintain written procedures for the:
 - identification,
 - documentation,
 - appropriate review, and
 - approval of changes affecting the quality of products and/or processes, equipment, systems, and methods.
- 2) Change control procedure should ensure that changes will be implemented in a controlled manner.
- 3) Anticipated changes should be evaluated to determine impact on component quality
 - Evaluation should determine if validation or revalidation is required

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IPAC-RS Guideline on Change Control: 9 Points

- 4) An independent group, such as the Quality Unit, should have responsibility and authority for management/approval of changes
- 5) For changes requiring customer notification, the customer must also approve the changes
- 6) Critical to notify, consult with, and seek approval of customers regarding changes that can impact component quality



IPAC-RS Guideline on Change Control: 9 Points

- 7) Customer and supplier should agree on notification of changes
- 8) Terms agreed should be reflected in a supply agreement and/or quality agreement
- 9) Suppliers should ensure that *their* suppliers have adequate change control programs in place



Supplier Perspective on Change Control

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Scope of Change Control

- Supplier's Change Control Process needs to address:
 - Raw materials suppliers
 - Raw material suppliers' processes
 - Raw materials
 - Sub-contractors
 - Facilities/Utilities
 - Manufacturing sites
 - Manufacturing processes

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Scope of Change Control

- Scope cont'd
 - Manufactured components
 - Manufacturing/testing equipment
 - Laboratory processes/procedures
 - Test methods
 - Components' documentation (specifications, filings, drawings, etc.)
 - Computer hardware/software packages affecting product

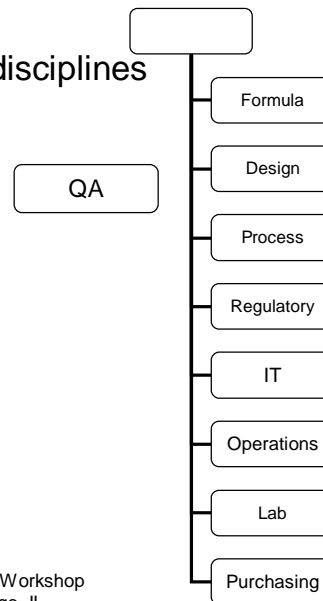
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Change Control is Cross-Functional

- Scope touches multiple supplier disciplines
 - Formula Development
 - Design Engineering
 - Process Engineering
 - Regulatory
 - Quality Assurance
 - IT
 - Operations
 - Laboratory
 - Purchasing



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Change Control Program Overview

- 1) Define Change
 - Change Request Number
 - Change Title
 - Change Type
 - Change Class
 - Description of Change
 - Priority (Standard / Like for Like)
 - Affected Process
 - Initiator
 - Initiator Location



Change Control Program Overview

- 2) Change Request to proceed for Approval
 - Area Management
 - Quality Assurance
- 3) Change Request routed to defined reviewers for approval



Change Control Program Overview

- 4) Review and approval process to execute change should address:
 - Ability to route to additional reviewers/approvers
 - Changes to documented change control information
 - Addition of needed supporting action items and/or change control “children”
 - Feedback mechanism
 - Document changes
 - Rejection of change

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Change Control Program Overview

- 5) Quality assurance reviews completed review request and provides final disposition to execute/not execute changes
- 6) Change control execution
 - Implement change
 - Complete defined action items
 - Complete defined change control children



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Change Control Program Overview

- 7) Completed change control and associated documentation forwarded for final disposition
 - Others
 - Quality assurance - last



Designing an Effective Change Control Program

- Team composed of representation from each participating area
 - Team Representatives provide input and agreement to standardize change control workflow
 - Considerations for multi-sites





Implementing an Effective Change Control Program

- Define change control process
 - Proceduralize
 - Approve
- Conduct and document training on process



Conclusion

- OINDP manufacturers and suppliers must discuss, understand, and agree on:
 - What constitutes a significant change
 - What type of changes require notification and/or approval
- These must be covered under a mutually agreed to Supply Agreement and Quality Agreement.



Questions?



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