

Pharmaceutical Quality System (ICH Q10) Conference
October 4-6, 2011 | Crystal Gateway Marriott | Arlington, Virginia
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The Effective Management of Change Across the ICHQ10 Lifecycle

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Change Management

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- This presentation will:
 - describe a structured approach to change across the ICH Q10 lifecycle
 - ❖ Pharmaceutical Development
 - ❖ Technology Transfer
 - ❖ Commercial Manufacturing
 - ❖ Product Discontinuation
 - describe the relationship between ICH Q10, ICH Q8 (Quality by Design) & Q9 (Quality Risk Management) for Change Management

Features of an Effective Change Control System 1

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- SOP that describes each of the key steps of:
 - ❖ Evaluation of a change
 - ❖ Approval to proceed with the change
 - ❖ Implementation of the change
 - ❖ Review to ensure that the change has been effective
 - ❖ Reviews effectiveness of overall system
- Clear accountabilities for each of these steps
- Considers upstream and downstream impact of change
- Prioritises urgent and important changes

Features of an Effective Change Control System 2

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- Employs effective use of risk management tools (ICH Q9) through the change cycle
 - Impact gauged by *probability, severity, detectability*
 - Use of prior knowledge – development, other manufacturing locations, similarities with other products
 - Output should include understanding of adequacy of controls and additional ones as necessary

Features of an Effective Change Control System 3

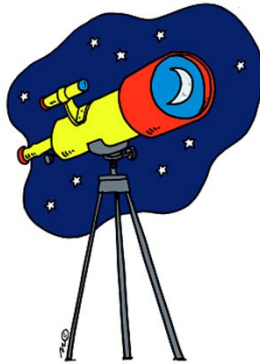
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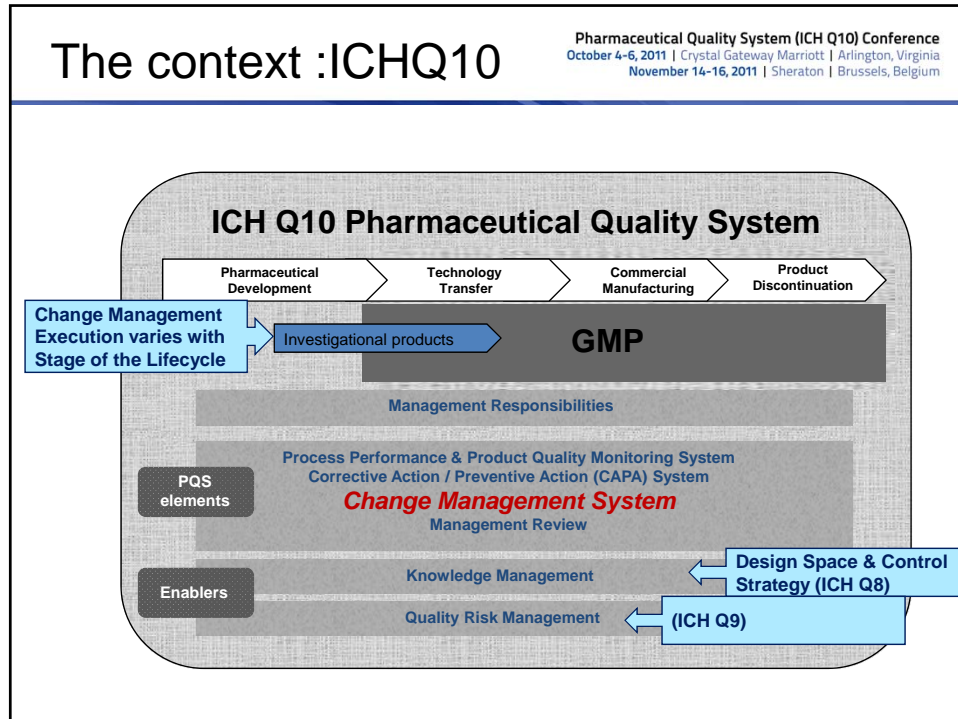
- Describes role of Quality Unit
 - Ensure change management system in place
 - Ensures IT system for change management validated
 - Approves changes – lifecycle dependent
 - Audits impact of changes
 - Reviews effectiveness of system and recommends improvement where necessary
 - Assures safety and quality of product

Change Management

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Scope is restricted to the management of change within the company quality system and therefore does not include changes to regulatory files

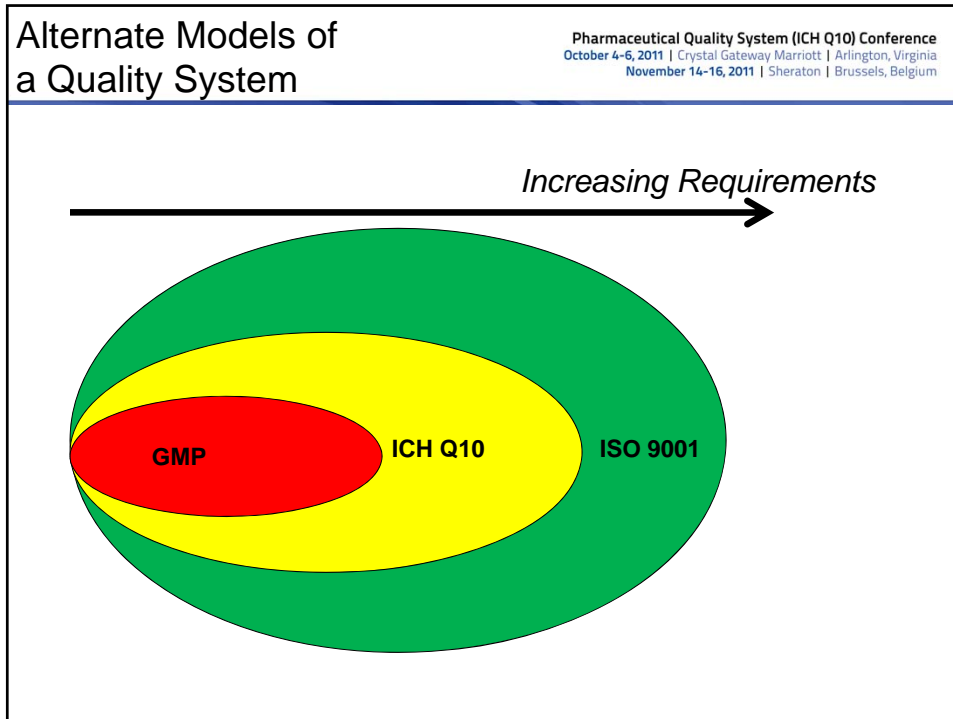




Change Management as a Root Cause?

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- "We are continuing to see these increased numbers for shortages, especially for older sterile injectable drugs," said Valerie Jensen, director of the FDA Drug Shortages Program.
- "The reasons for the shortages vary. Some drug manufacturers are discontinuing older drugs and replacing them with newer ones, which are usually more profitable, according to the FDA. They are also recalling some drugs because of quality problems"



Differing System Requirements

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Quality System Feature	GMP	ICH Q10	ISO9001
Quality Risk Management	✓	✓	✓
Quality by Design	-	Optional	Optional
Product & Manufacturing Process Performance			
• In- process and end product testing	✓	✓	✓
• Establish control strategy to facilitate timely feedback / feed forward, measure, analyse, identify sources of variation, and drive continual improvement	✓	Also supported by ICH Q8 & Q9	Also supported by ICH Q8 & Q9
Business Process Performance (e.g. Finance)	-	-	✓
Knowledge Management	-	✓	✓
Senior Management Responsibilities			
• Production and QC unit	✓	✓	✓
• Accountability for PQS including governance and reviews, establish Quality Policy and Quality Objectives	✓	Enhanced by Q10	✓

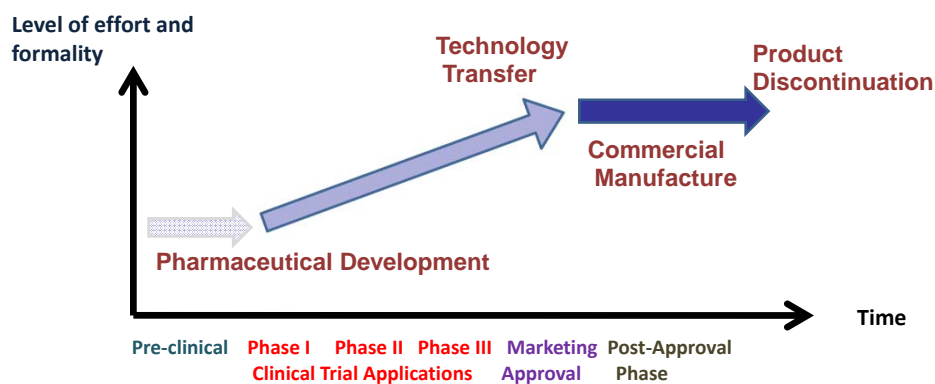
Change Management System Principles

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- Whichever quality system a company adopts it must have a change management system in place
- The extent of application of the change management system will vary depending on the stage of the lifecycle described in ICH Q10
 - general principle of increasing requirements for change up to and including commercial manufacturing
 - specific requirements for product discontinuation

Change Management System Principles

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Formality of Change Management Approach Ramps Up Over Product Lifecycle

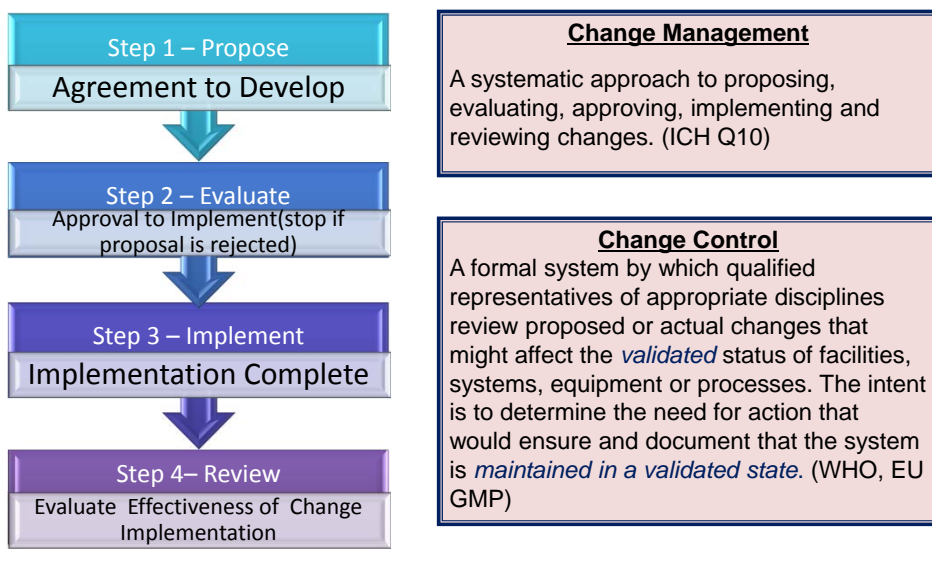
Change Management Model

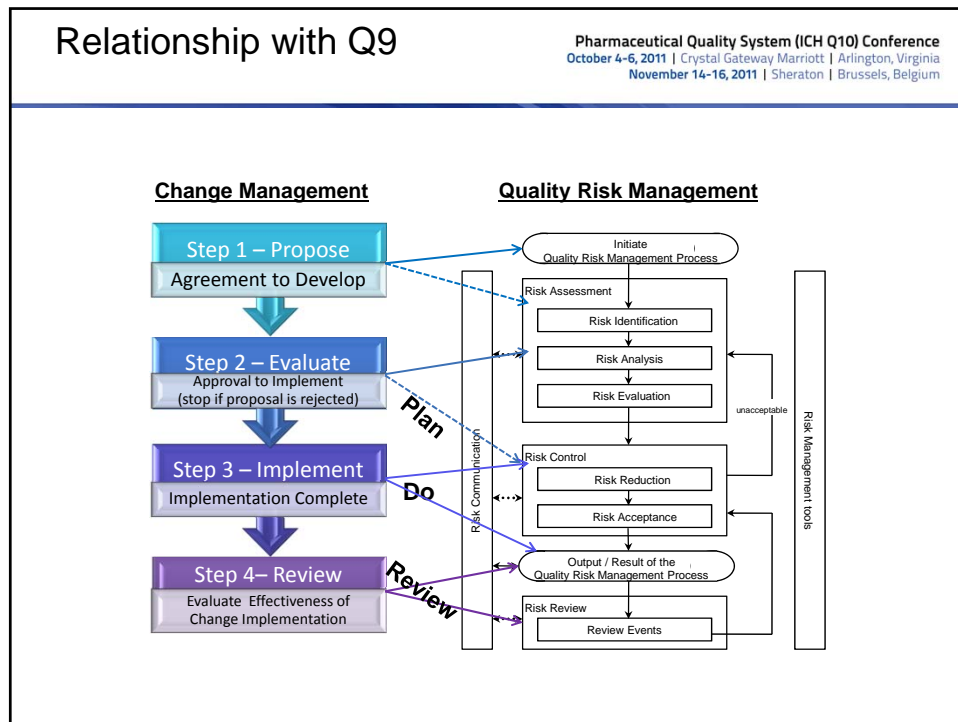
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- A systematic toll-gate model to ensure that individual changes are *evaluated, approved, implemented and reviewed (ICH Q10)* regardless of stage in the lifecycle
- The extent of formality is related to the stage in the ICH Q10 lifecycle
- Enables effective use of elements of ICH Q8, and Q9, in change management model

Change Management Model

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Change Management Roles

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Clear Accountability for the Change Management System e.g. Process Steward (QA)

- Could be “local” (e.g. site based) versus “global” (e.g. multi-site) change
- Could have wider accountability for other parts of the quality system
- Owner of Change Management and Portfolio of Change Projects
- Key individual in Knowledge Management
- Chair or secretary of multi-disciplinary Change Review Board /Team

Pharmaceutical Development

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- Change is an inherent part of the development process and should be documented – good scientific practice
- The formality of application of the change management process should be consistent with the stage of pharmaceutical development – greater for phase III.
- Clinical Trial Manufacture and Supply – co-location
- Potential impact on INDs/CTAs as knowledge is acquired.
- Changes could be incorporated and tracked through the development plan

Technology Transfer

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- Technology Transfer may occur at different points in the lifecycle e.g. prior to phase III clinical manufacture, post approval to additional or alternative manufacturing site.
- Technology Transfer forms the basis for commercial manufacturing and supply and associated practices of QbD and Control Strategy
- GMP standards approximate to commercial manufacture and full application of the change management model is advocated
- Changes could be incorporated in the Technology Transfer plan
- Need to consider impact on emerging or approved regulatory filings
- Impact on existing facilities (if not new build or dedicated)

Commercial Manufacture

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- Full GMP standards apply and full application of the change management model is advocated
- Extent of markets supplied and different GMP requirements need to be considered during change management (and impact on regulatory filings)
- Impact of upstream activities e.g. component and raw material supplies
- Impact on downstream activities e.g. subsequent manufacturing packing and distribution steps

Product Discontinuation

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- Product Discontinuation is the removal of a product from commercial supply i.e. the complete cessation of all manufacturing, release and supply activities.
- The sale or transfer to another manufacturing unit, including third parties is considered to be captured under technology transfer.
- Consideration to patient impact and planning for discontinuation e.g. interaction with regulators
- Product Discontinuation signifies the end of the Q10 lifecycle.

Design Space & Control Strategy

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- Change Management model should be applied for all change proposals
 - movement within the Design Space is not a regulatory filing change
 - file variation/supplement if movement is beyond design space
- Control Strategy
 - any potential impact on control strategy should be carefully evaluated before proceeding
 - consideration to regulatory file variation/supplement should be evaluated

Thanks

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- Lilian Hamilton/Claire Myles (AZ)
- Susan L Schebler– Lilly
- Mike James- GSK
- Ron Taticek –Roche/Genentech
- Michael Choi – Cephalon
- Bernd Boedecker – German Inspectorate
- Gregory Tewalt – Amgen
- Takeshi Takashima –Powrex/ISPE Japan

