ICH Q12 - Technical and Regulatory Considerations for Pharmaceutical Product Lifecycle Management

Training Material
Module 0 – Setting the Scene

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Legal Notice

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ICH Q12 – Overview Training Material

- **Module 0 – Setting the Scene**
  - Review of previous ICH guidelines (scientific basis for ICH Q12)
  - ICH Q12: Rationale and Objectives
- **Modules 1-7**
  - Presentation of Content in the ICH Q12 Guideline
  - Examples from the Annex
- **Module 8**
  - Additional Examples and Practical Recommendations

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Quality Statement - Brussels 2003

"*Develop a harmonised pharmaceutical quality system applicable across the lifecycle of the product emphasizing an integrated approach to quality risk management and science."*

- Included in this statement are three important elements over the lifecycle of a product:
  - Science and technology
  - Quality risk management
  - Quality system
- Scientific progress and innovation do not stop at time of submission and/or first marketing authorization, but continue during commercialization of the product. These processes are, together with quality risk management and the pharmaceutical quality system, the basis for continual improvement.

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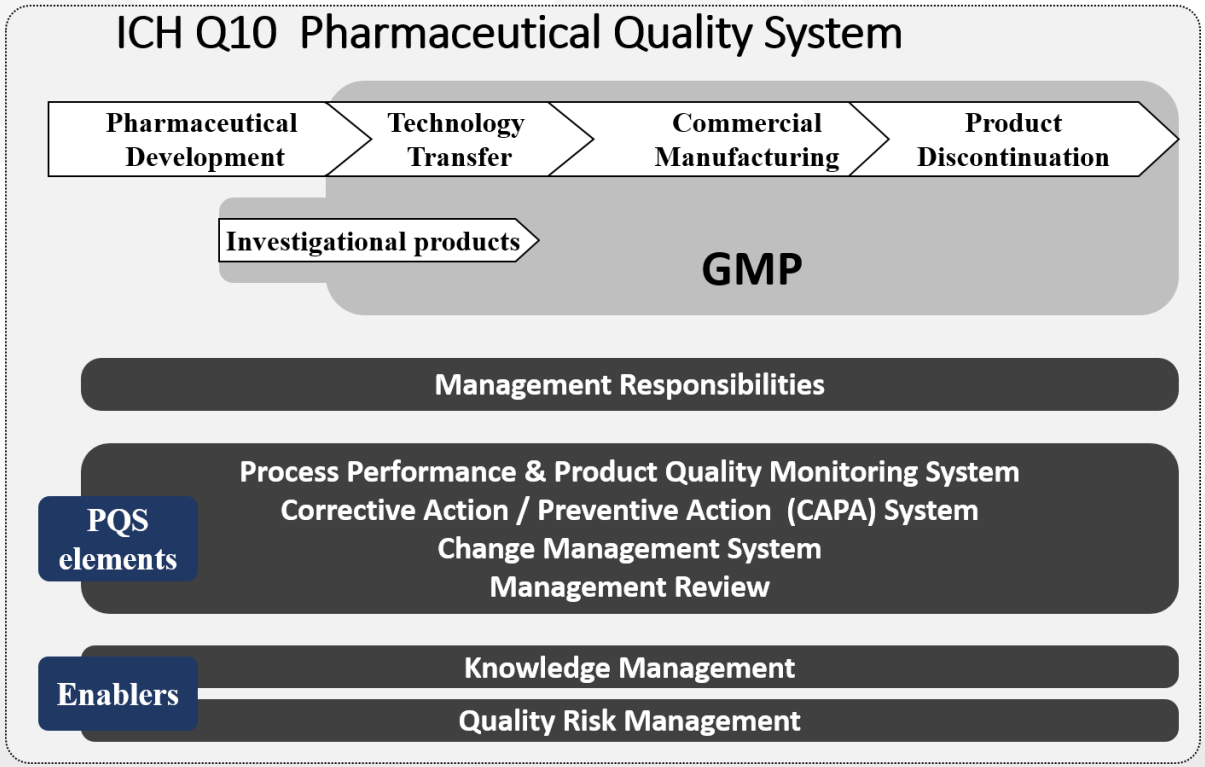
Lifecycle

The lifecycle of a product or process starts at development and continues during the pre- and post-approval phases, including commercialization and product discontinuation (see figure below)

Diagram ICH Q10: Lifecycle and Enablers



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Lifecycle

- ICH Q12 deals specifically with the post-approval phase
- Early contact with regulators is recommended during development and pre-approval phases
  - These phases of the lifecycle are important because they facilitate and influence the post-approval phase
- The figure on the next slide, "*Lifecycle Definition* and Process Flow,"* describes the interaction between regulators and industry during the life-cycle starting with the pre-approval phase (development), moving through the approval phase (marketing application), and ending with the post-approval phase

*Note: ICH Q12 does not address product discontinuation

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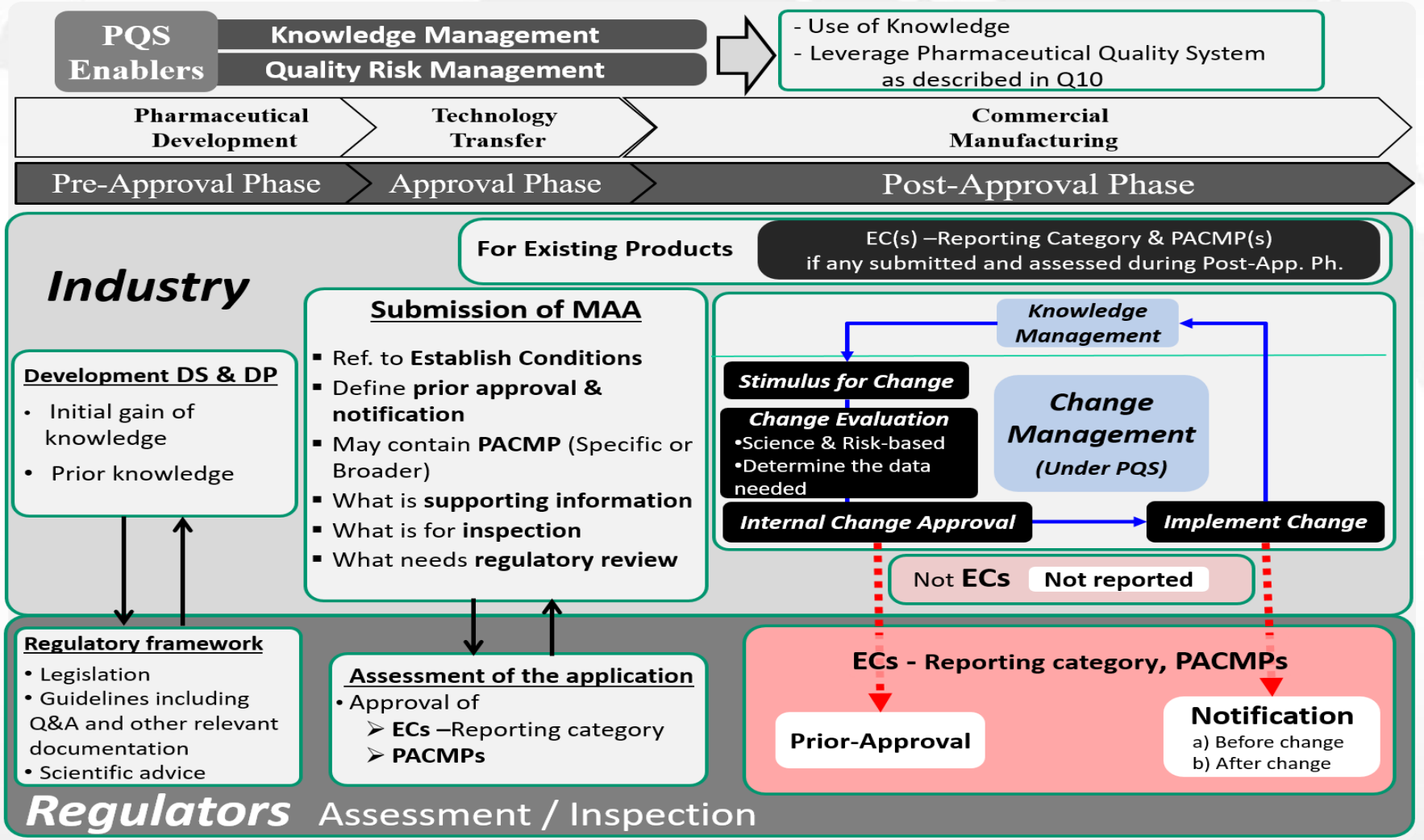
Life-Cycle Definition and Process Flow



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ICH Q8 (R2): Pharmaceutical Development

- The aim is to design a quality product and its manufacturing process to consistently deliver the intended product performance
- An applicant might choose either an empirical approach (minimal) or a more systematic approach (enhanced) to product development, or a combination of both approaches
- A greater understanding of the product and its manufacturing process (determining the functional relationships that link material attributes and process parameters to product Critical Quality Attributes) can create a basis for more flexible regulatory approaches
- No matter which development approach is chosen, the product should always meet patients' needs

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ICH Q11: Development and Manufacture of Drug Substances

- Similar to ICH Q8 for the drug product, ICH Q11 provides recommendations for the development and manufacture (synthesis) of the drug substance
- Similar principles and concepts apply

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ICH Q9: Quality Risk Management Process

- Quality Risk Management (QRM) is a valuable component of an effective Quality System
- *Risk* is defined as the combination of the probability of occurrence of *harm* and the *severity* of that harm
- QRM is an essential aspect of change management enabling identification and evaluation of the impact to quality of a change
- The following figure shows an overview of a typical quality risk management process

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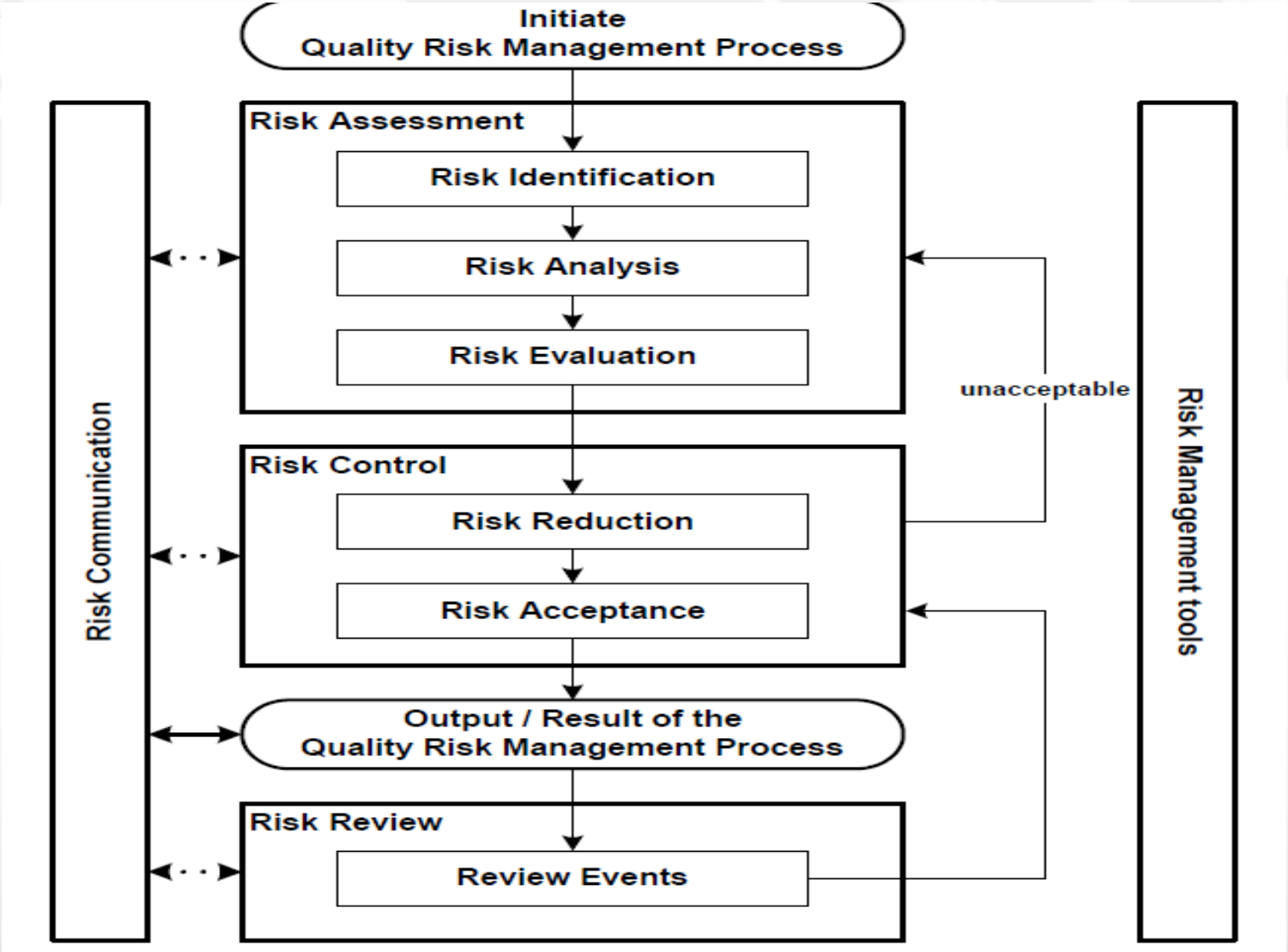
ICH Q9: Quality Risk Management Process



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ICH Q10: Pharmaceutical Quality System

- A Quality System (QS) is defined as the sum of all aspects of a system that implements quality policy and ensures that quality objectives are met (ICH Q9)
- An effective QS has to be implemented all along the supply chain
- The Pharmaceutical Company's quality system should include appropriate processes, resources and responsibilities to provide assurance of the quality of *outsourced activities* and purchased materials
- Not a new requirement: all changes (regulatory changes or not) have to be performed under a quality system

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Why a guideline on Lifecycle Management?

- The lifecycle of a pharmaceutical product and its corresponding manufacturing process is a dynamic process, meaning that the evolution of a product/process does not stop after first approval

- Post-approval changes can be influenced by:
  - Additional experience gained during commercial phase
  - Scientific progress
  - Change in Regulation

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Why a guideline on Lifecycle Management?

- As a consequence, the management of post-approval changes is an essential aspect of the lifecycle of the product/process
- Potential benefit of post-approval changes:
  - Ensures continual improvement of product and process
  - Product and process remain up to date with the current scientific knowledge
  - Reduction of costs and resources
  - Ultimately ensures supply of medicines

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Why a guideline on Lifecycle Management?

- Challenge:
  - Regulatory processes for requesting product changes may be complex and are not necessarily harmonized between regions
  - Diverse regional regulatory environments often prevent change to a marketing authorization within a reasonable timeframe
  - Some changes are not performed due to the time needed for their global implementation
- The objective of ICH Q12 is to help overcome this situation and facilitate the continual improvement of drug quality

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Rationale-Background

- ICH Q12 provides recommendations on how to manage post-approval changes
- Changes to manufacturing processes and products depend on the level of scientific knowledge and technical understanding
- The greatest benefit from the ICH Q12 guideline comes when it is applied in conjunction with other ICH “Q” guidelines, including:
  - ICH Q8 (R2) Pharmaceutical Development
  - ICH Q9 Quality Risk Management
  - ICH Q10 Pharmaceutical Quality System
  - ICH Q11 Development and Manufacture of Drug Substances
  - ICH Q5E Comparability of Biotechnological/Biological Products Subject to Changes in Their Manufacturing Process

ICH Q12 Objectives and Benefits

- The objective of ICH Q12 is to facilitate the management of CMC post-approval changes in a more predictable and efficient manner across the product lifecycle, mainly in the area of frequent manufacturing changes, including analytical methods
- Full implementation of ICH Q8, Q9, Q10, and Q11 is not a prerequisite to using Q12
- Caution:

  Q12 is not only about flexibility. Following Q12 concepts and principles, supported by sound product/process development, will lead to a more transparent post-approval submission.

ICH Q12: Table of Contents

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B. Annexes

Annex I: Illustrative Examples

IA/IB: ECs for the manufacturing process

IC: ECs for analytical methods

ID/IE: PACMPs

IF: PLCM

Annex II:

Structured approach to analytical procedure changes

The annexes contain examples illustrating the information provided in the core guideline