

M4Q(R2) – An Industry Perspective

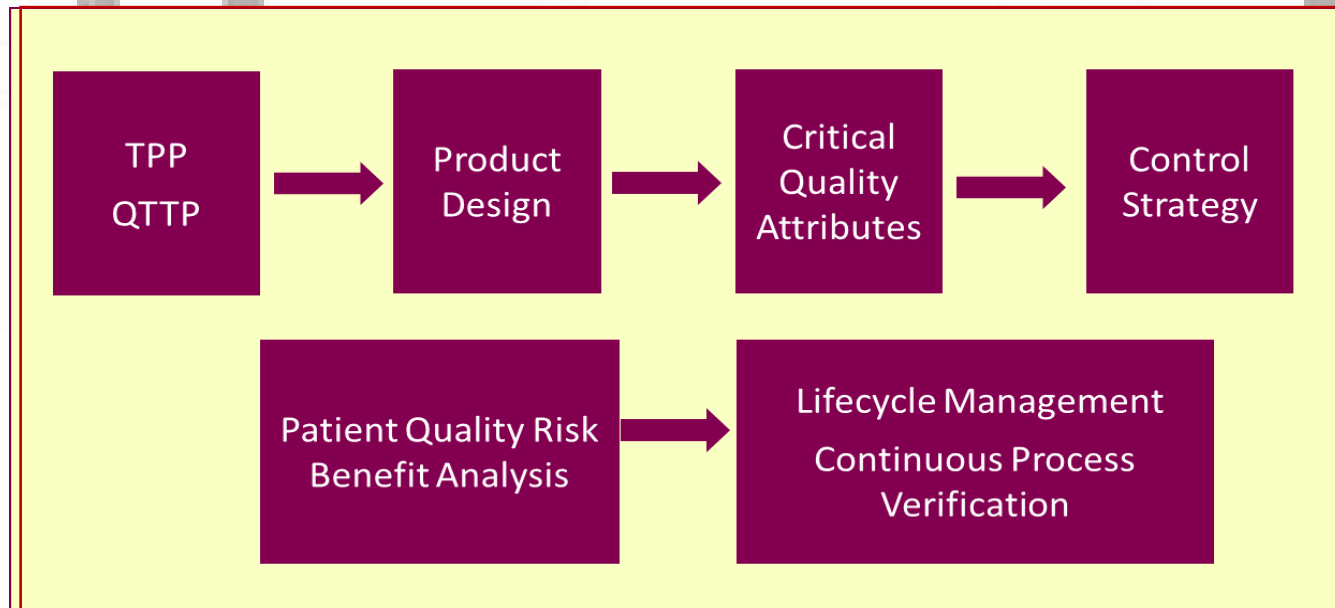
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A Vision: Building a Bridge to the Patient



Data
(Module 3)



Patient

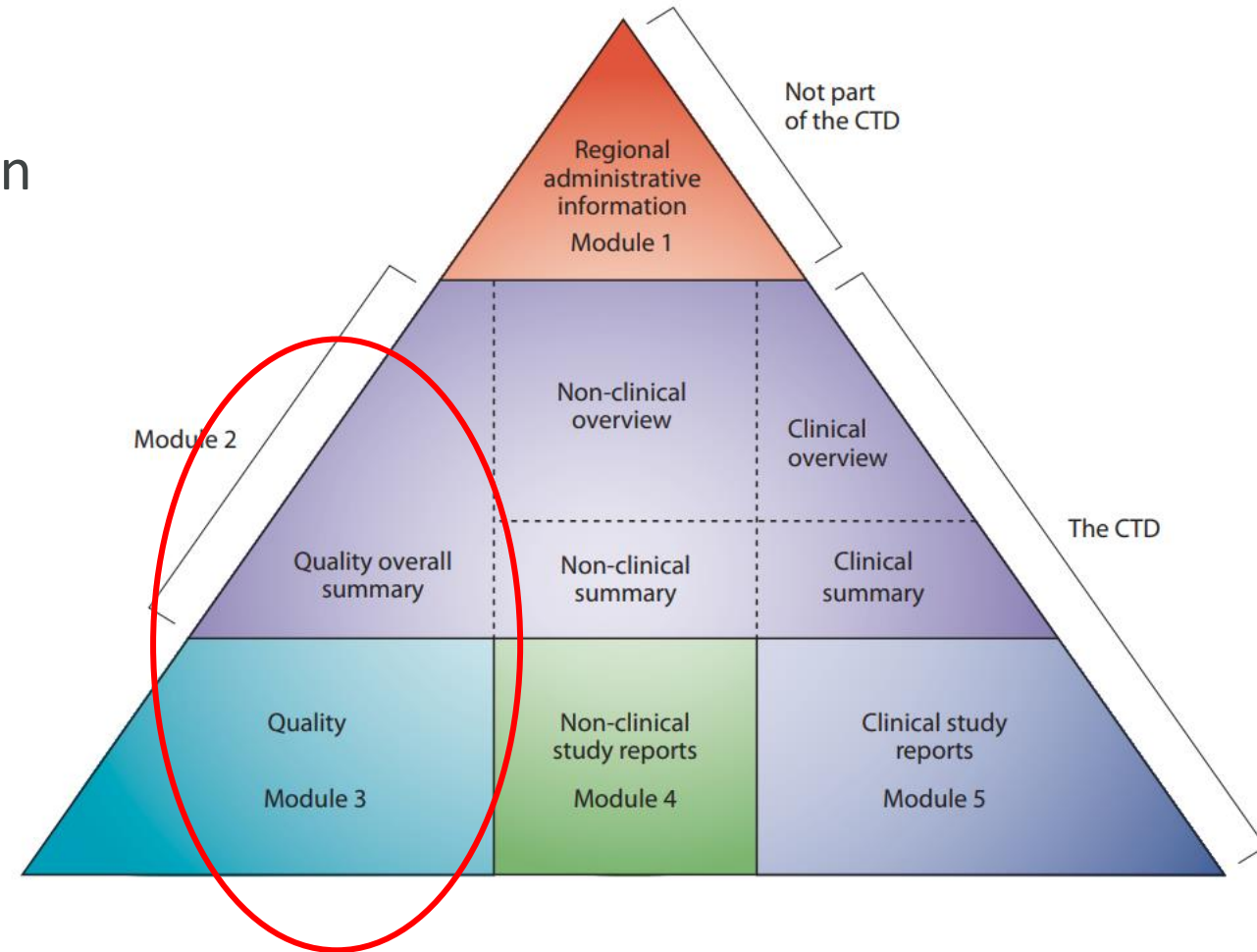
Module 2 Narrative/Summary bridging to the Patient

Benefits of Building Module 2 as the Bridge

- **Provides a globally standardized approach for Module 2.**
- **MAA's**
 - CMC risks described in a patient risk/benefit, globally accepted, standard framework.
 - Summarize overall control strategy, link QTTP and CQAs to control strategy, facility assessment and utilize principles of Q9 as it relates to the patient risk benefit.
 - Cutting across all ICH Quality Guidelines to ensure a common regulatory assessment and thereby facilitate review by global regulators and worksharing/mutual reliance
- **Post Approval Changes**
 - Update the patient risk/benefit assessment as the knowledge is gained of the product throughout the lifecycle.
 - Utilize principles of ICH Q12, for example Lifecycle Management
 - Update of the PLCM and established conditions.

What's M4Q Designed to Do?

- ▶ Provides a harmonized structure and format for presenting quality information in Common Technical Document (CTD)/electronic CTD for registration of pharmaceuticals for human use
 - **Module 2 Quality Overall Summary (QOS)**
 - **Module 3 Quality**



ICH chose a step-wise approach to modernise M4Q

- ▶ ICH M4Q(R2) will define the new structure of Module 2.3 and Module 3
- ▶ When M4Q (R2) has reached step 2, a concept paper outline for the work on Structured Product Quality Submissions (SPQS) will be made
- ▶ Therefore, M4Q(R2) will think ahead but not work on implementation of structured data

ICH M4Q(R2) Concept paper



Concept Paper

M4Q(R2) Common Technical Document on Quality Guideline

Endorsed by the Management Committee on 15 November 2021

Type of Harmonisation Action Proposed

Revision of Existing Guideline

Statement of the Perceived Problem

Introduction of the Quality - M4Q(R1) guidelines on the Common Technical Document (CTD) in 2002 harmonized the format of quality information for registration of pharmaceuticals for human use and offered great benefits to industry, regulators, patients, and consumers. M4Q(R1) is now due for revision to further improve registration and lifecycle management efficiency, leverage digital technologies, and accelerate patient and consumer access to pharmaceuticals. The specific drivers for this revision include:

1. Several ICH regions have not fully implemented ICH M4Q(R1). The modernization will support and clarify global understanding of the CTD, enabling greater regulatory convergence and harmonization, and decrease redundancy.
2. The M4Q(R2) guideline should align with modern quality guidelines Q8-Q14, and other relevant ICH guidelines that have been developed or given greater focus since the issuance of ICH M4Q(R1).
3. The M4Q(R2) guideline should provide guidance on the location of information supporting multicomponent and/or complex products such as antibody-drug

Expected future completion date	Milestone
Sep. 2023	Consensus EWG first draft of technical document
Oct. 2023	Plenary Working Party (PWP) Consultation
Nov. 2023	Step 1 Experts sign-off
Nov. 2023	Step 2a Endorsement by Members of the Assembly Step 2b Endorsement by Regulatory Members of the Assembly Release for public consultation
April-July, 2024	Public workshops on introduction of M4Q(R2) Step 2 in Asia, EU, and America
Nov. 2024	Review and resolve public comments
May. 2025	Step 3 Sign-off and Step 4 Adoption of Final Guideline

What Are the Issues to be Resolved?

1. Expanding the scope of M4Q(R1) guideline. This M4Q(R2) guideline applies to all pharmaceutical drug substances and products that require a marketing authorization
2. Establishing the role of M4Q(R2) as the main source of the structure and location of regulatory quality information. The guideline should specify the location of lifecycle management elements. It should address diversity in requirements for quality information across ICH regions and streamline the requests for PQS and GMP information
3. Organizing product and manufacturing information in a suitable format for easy access, analysis, and knowledge management. The revision should facilitate inclusion of information supporting emerging concepts

What Are the Issues to be Resolved (Continued)?

4. Incorporating concepts and data expectations presented in ICH Quality guidelines and aligning with currently recognized international standards and guidelines. The M4Q(R2) should enable better use of prior knowledge and ensure that the level of detail and data of the dossier is commensurate with the risk to the product's quality
5. Organizing product and manufacturing information in a suitable format for easy access, analysis, and knowledge management. The revision should facilitate inclusion of information supporting emerging concepts
6. Enhancing the Quality Module 2 to facilitate the efficiency and effectiveness of regulatory submissions and assessments. The Quality Module 2 may discuss product quality benefit-risk considerations, summarise the pharmaceutical development, and present an overall understanding of the product quality

M4Q(R2) Objectives

- ▶ M4Q(R2) guideline will improve submission and assessment efficiency, resulting in accelerated access to pharmaceuticals by (6Es):
 1. Encouraging **global convergence** of science- and risk-based regulatory approaches in the preparation of dossiers.
 2. Explaining and defining the **organization and positioning of information for Modules 2 and 3.**
 3. **Enriching communication between regulators and applicants and enhancing lifecycle and knowledge management.**

M4Q(R2) Objectives (Continued)

4. Embracing product and process **innovation**
5. Enabling efficient use of **digital tools** for submission and assessment and preparing for the closely linked, upcoming ICH guideline on structured pharmaceutical quality submission
6. Elucidating regulatory expectations and supporting **efficient** assessments, decision-making, and actions

M4Q(R2) Importance for Industry

- ▶ M4Q(R2) guideline would be of great benefit to industry.
 - For industry, it would clarify regulatory expectations, facilitate applying the enhanced ICH quality strategy/vision, streamline regulatory application preparation, improve the quality of submissions, facilitate data and information management, promote communication with regulators, and foster harmonisation and standardisation of data/information requirements for regulatory submissions, while increasing regulatory convergence

Industry objectives

- Global harmonisation of CMC documents and submission
- Streamline GMP documents in the dossier
- Enable full use of ICH Q8-Q14
- Enable new product modalities and new technologies
- Prepare for structured data submission
- Tell the product story and link it to the patient

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