Update on ICH M4Q(R2) and Industry perspective

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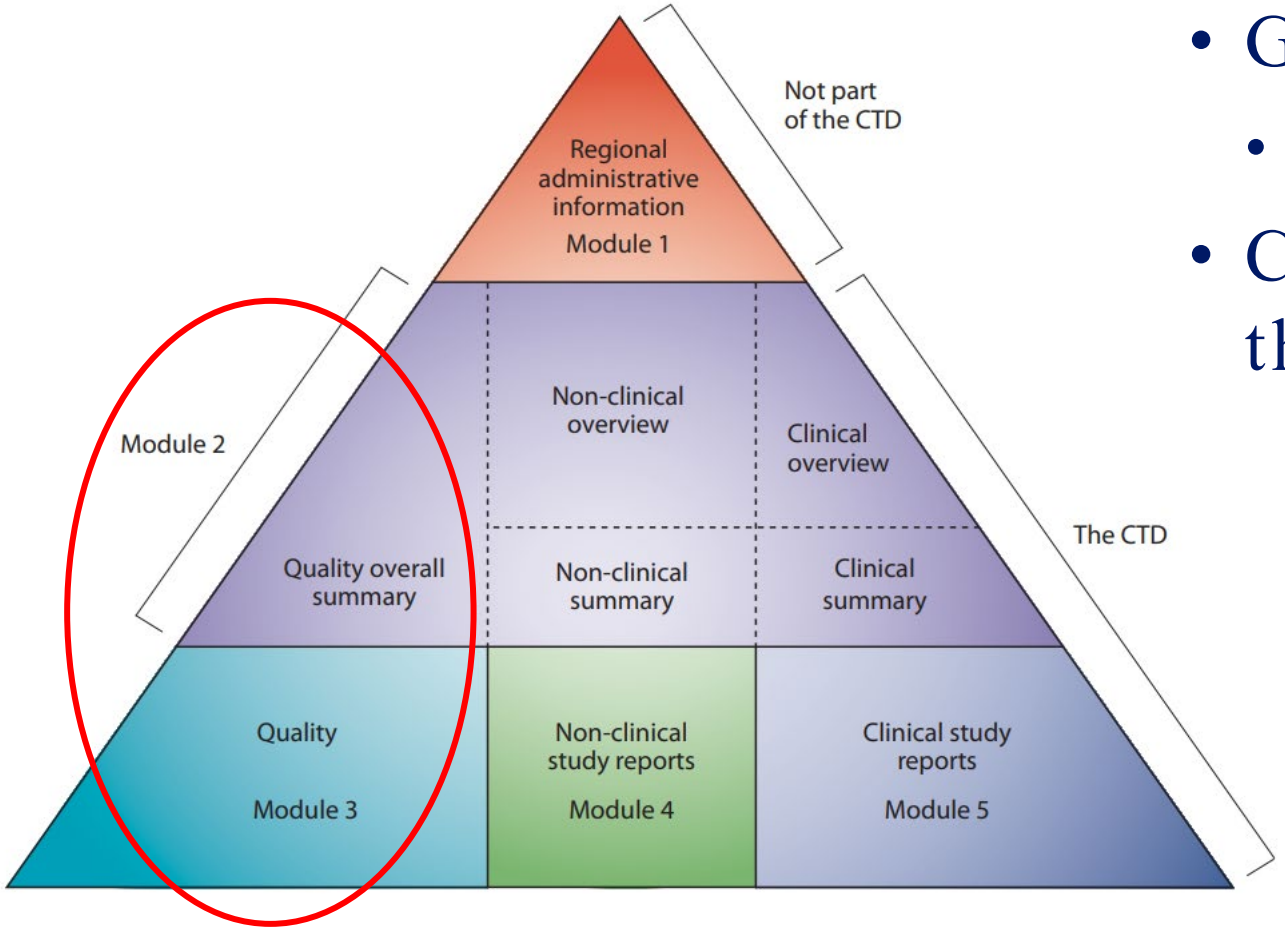
Advantages of the CTD (Common Technical Document)



- Globally harmonised
  - Except for regional requests
- Clear location of documents in the application

→ **Faster access for patients**

M4Q(R1) was developed in 2002 and needs updating!

ICH M4Q(R2) Concept paper

ICH
harmonisation for better health

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

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

The M4Q (R2) guideline will be a foundation for Digital Transformation in Regulatory Affairs

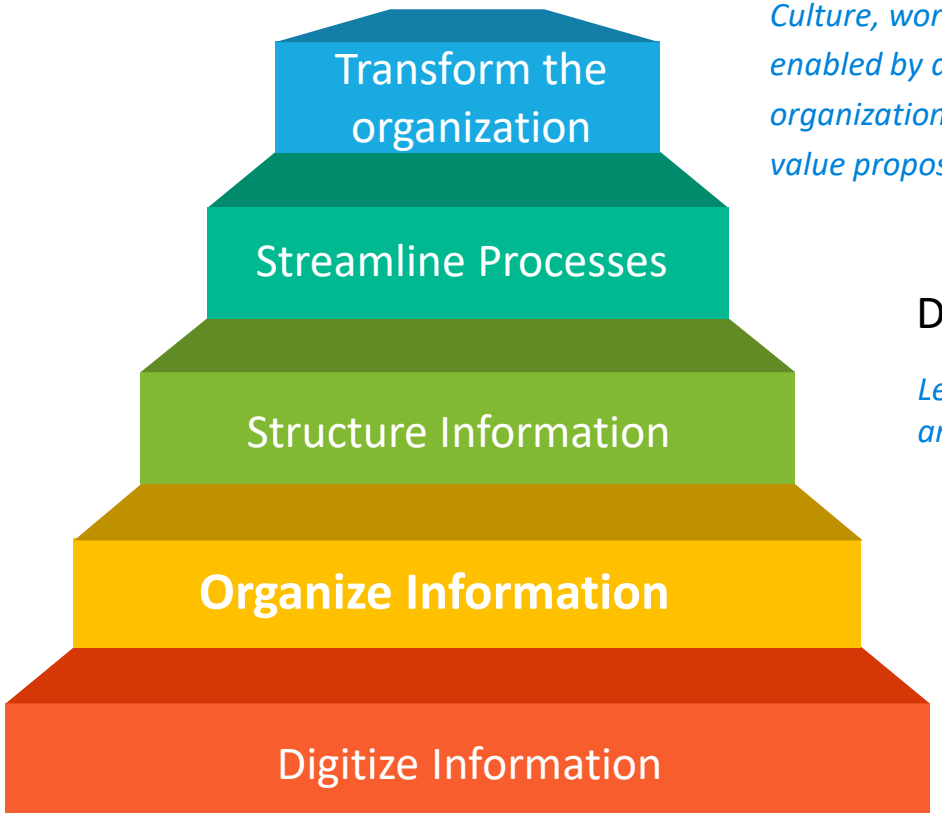
Dynamic Regulatory Assessment Cloud Submissions/Accumulus Synergy

Data Analytics Support, KASA, UNICOM, Variation Automation

IDMP+SPOR, PQ-CMC

CTD + eCTD

Paper to PDF



Digital Transformation

Culture, workforce, and technology shifts enabled by digitalization that transform an organization's operations, strategic direction, value proposition

Digitalization

Leveraging digital technologies and information and automation to improve processes

Digitization

Changing from analog or physical to digital form

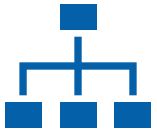
ICH chose a step-wise approach to modernise M4Q

- 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

Potential for M4Q

The new organisation of information can bring us far in this transformation

Reflect the latest thinking on innovative medicine development, production and control



Introduce a conceptual model that better conveys product knowledge and experience

Reduce ambiguity and leverage global standards to break information silos across domains and regions

Enable knowledge management and data analysis to increase efficiency for industry and regulators

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. Better capturing the pharmaceutical development and the proposed overall control strategy, which should be the backbone of the revised M4Q structure. This should address key elements of the proposed pharmaceutical product, including the Quality Target Product Profile (QTPP), manufacturing process, and overall control strategy
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

Industry Objectives for M4Q (R2)

- Global harmonisation of CMC documents and submission
- Minimise 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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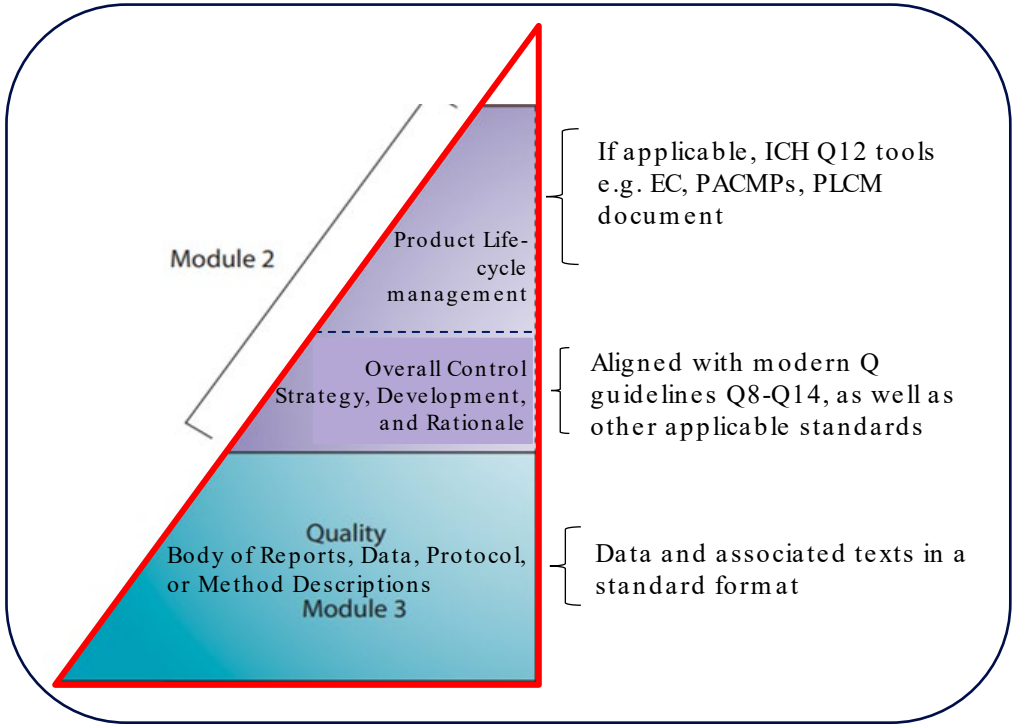
M4Q(R2) Conceptual Thinking

Current thinking of the EWG

Industry

- ICH Q12 tool such as Established Conditions to maintain quality over product lifecycle
- Tells the product story and relates to patients
- Better captures the pharmaceutical development and the proposed overall control strategy
- Risk-based approach with focus on patients

- Prepare for submission of Structured Product data in Module 3



Authority

- Transformational Module 2 serves as a basis for efficient and effective regulatory assessment as well as reliance-based approval
- Risk-based approach with focus on patients
- Product benefit- quality risk considerations

- Module 3 data to easy access, analysis and knowledge management
- Follows standard format to be conducive to structured data

M4Q(R2) establishes Module 2 as the basis for regulatory assessment, supported by Module 3

Current thinking of the EWG

M4Q(R2) establishes M2 as the basis for regulatory assessment, supported by M3

Module 2

- Basis for regulatory assessment
- Comprehensive overview of the product and its components
- Presents and discusses critical information
- PLCM tools

Links for further details

Module 3

- Information and data repository incl. reports, data, protocols, descriptions
- Prepared for SPQS
- Supporting emerging concepts

- M4Q(R2) should enable efficient, effective, patient-centric and globally harmonised submissions, assessment and life cycle management, and minimize dossier redundancies
- Suitable for various types of submission and product modalities

Current thinking of the EWG

Role and Objectives of Module 2 and 3 in Submission and Assessment

- M4Q(R2) CTD on Quality Guideline consists of Module 2 (M2) and Module 3 (M3) in a holistic and complementary manner with minimum duplication between these two modules.
- It establishes M2 as the basis for regulatory assessment, supported by M3.
- Risk-based principles are used to focus on critical quality elements.
- M4Q(R2) should be suitable for various types of submissions and complex modalities and technologies

In summary, M4Q(R2) should enable efficient, effective, patient-centric and globally harmonised submissions, assessment and life cycle management, and minimize dossier redundancies.

Current thinking of the EWG

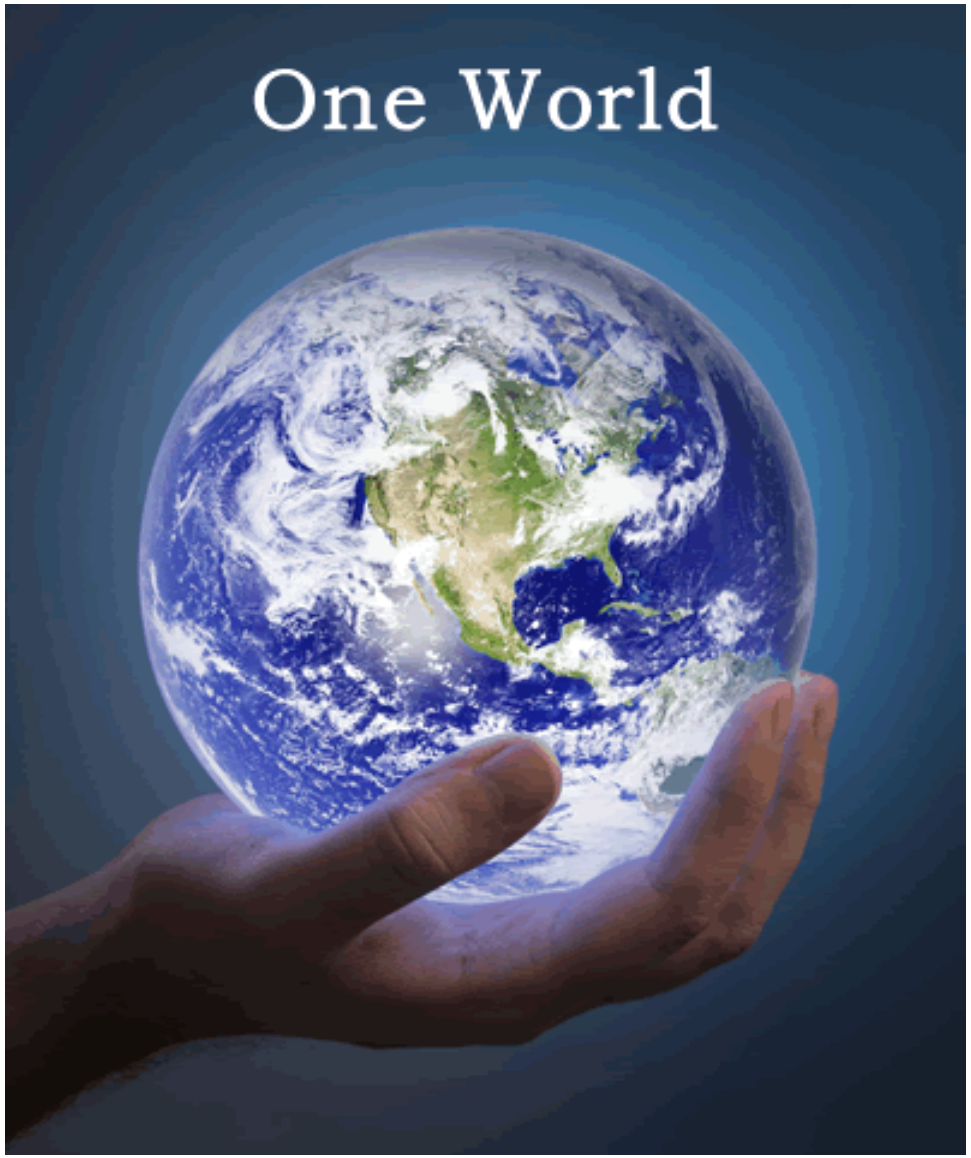
Module 2

- M2 should provide a sufficiently comprehensive overview of the pharmaceutical product and its components.
- It should provide a basis for an efficient and effective regulatory submission and assessment, and product-life cycle change management.
- M2 may also support reliance-based approval.
- M2 presents and discusses the critical information, thereby providing a common understanding of the product and manufacturing process factors determining quality as well as providing product quality benefit-risk considerations.
- It may also include Product Life Cycle Management tools as per ICH Q12 guideline.
- M2 may guide the reader how the information is presented throughout the quality part of the dossier.

Current thinking of the EWG

Module 3

- M3 serves as the information and data repository that supports M2 and is presented in a globally standardized/harmonized format.
- M3 should lay the foundation for the Structured Product Quality Submission.
- M3 may comprise detailed information complementary to M2, such as reports, data, protocol, or method descriptions and should be organised in a suitable format for easy access, analysis, and knowledge management.
- Both M2 and M3 should facilitate inclusion of information supporting emerging concepts, such as advanced manufacturing, IT/software components, digitalization, data management, artificial intelligence/machine learning, and advanced analytical tools, to support regulatory assessment.



Harmonization and collaboration bring all regions and stakeholders closer together for the benefit of patients

Acknowledgement

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- EFPIA M4Q team


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