

## 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 conjugates, vaccines, ATMPs/Cell & Gene Therapies & Tissue Engineered Products or combination products that meet the definition of a pharmaceutical or biological product.
4. The M4Q(R2) guideline should facilitate leveraging advances in digital tools, data management and standardization, and analytics to enhance efficiencies and effectiveness of regulatory submissions and assessments, although the structured pharmaceutical quality submission is beyond the scope of M4Q(R2) guideline.

#### Issues to be Resolved

The focus of M4Q(R2) is the revision of CTD Quality sections in Modules 2 and 3 to capture quality information for the registration and lifecycle management of pharmaceuticals for human use. The main issues to be resolved during this revision include:

1. Expanding the scope of M4Q(R1) guideline. This M4Q(R2) guideline applies to all pharmaceutical drug substances and products (both chemical and biological) that require a marketing authorization. These may include multicomponent and/or complex products, such as antibody-drug conjugates, vaccines, ATMPs/Cell & Gene Therapies & Tissue Engineered Products or combination products that meet the definition of a pharmaceutical or biological product.

## *M4Q(R2) Concept Paper*

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 such as advanced manufacturing, digitalization, data management, artificial intelligence, and advanced analytical tools.
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. It may also include elements of the product and process development and understanding.
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, which may include risk and criticality assessment as per available Quality guidelines. The Quality Module 2 may also incorporate key elements of ICH Quality guidelines including lifecycle management tools to ensure product safety, efficacy, and quality.

### **Background of the Proposal**

#### 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.
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.

#### Importance

M4Q(R2) guideline would speed up patients and consumers' access to pharmaceuticals while being of great benefit to both industry and regulatory agencies.

## *M4Q(R2) Concept Paper*

1. For patients and consumers, it would ensure rapid and continuing access to new products by bringing a streamlined and consistent approach to the registration and lifecycle management of pharmaceuticals.
2. 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.
3. For regulators, it would enhance benefit-risk considerations, increase access to quality data and information, streamline regulatory assessment, facilitate oversight of pharmaceutical product quality, increase consistency and efficiency in regulatory decision-making and actions, and improve communication with industry and among regulators.

### Feasibility

M4Q(R2) will require a significant effort but is worthwhile given the importance and positive impact for patients and consumers, industry, and regulatory agencies. The development of M4Q(R2) will require ICH resources within the Quality category only, and therefore, it is feasible.

### **Type of Expert Working Group and Resources**

The Expert Working Group (EWG) will include regulators and industry representatives with innovative thinking and adequate expertise and experience in technical and regulatory issues associated with the quality parts of regulatory submissions. It should also consist of members with a working knowledge of solutions and tools for managing and analyzing structured data, as well as experts with GMP/inspection background.

### **Timing**

The anticipated time to complete the revision of the guideline will be 3-4 years.