Business Plan

M4Q(R2) Common Technical Document on Quality Guideline

Endorsed by the Management Committee on 15 November 2021

1. The issue and its costs

- *What problem/issue is the proposal expected to tackle?*

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 main issues to be tackled 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.
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.

- *What are the costs (social/health and financial) to our stakeholders associated with the current situation or associated with "non action"?*

  The development of ICH quality guidelines, along with advances in pharmaceutical science, manufacturing technology, and data management and analytics has motivated ICH to modernise the M4Q(R1) guideline. During the discussion of ICH Quality Guidelines such as Q8, Q12, and Q13, pharmaceutical industry and regulatory agencies recognized the limitation of the current M4Q(R1) format. Further, there is a growing divergence in regulatory expectations among ICH members/observers. Therefore, any delay in revising the M4Q(R1) guideline will hinder global convergence and information sharing, prevent advancement to a user-friendly structured application that will further enhance the efficiency and effectiveness of regulatory submission and assessment, and delay regulatory decision-making and actions, and therefore, accessibility of medicine to patients and consumers.

2. Planning

- *What are the main deliverables?*

  The main deliverable is a revised M4(Q) guideline, ICH M4Q(R2), Common Technical Document on Quality Guideline.

- *What resources (financial and human) would be required?*

  The Expert Working Group (EWG) includes approximately 30 experts. We anticipate the need for six face-to-face meetings and multiple interim video meetings to complete the revision of M4Q guideline.

- *What is the time frame of the project/milestones?*

  The revised guideline is anticipated to take three years to achieve Step 4, from December 2021 to December 2024.

- *What will be the key milestones?*

  2021: Final Concept Paper and Business Plan
  2022: Face to face EWG meetings and ICH M4Q(R2) Step 1.
  2023: Face to face EWG meetings and ICH M4Q(R2) Step 2 and Step 3.
  2024: Face to face EWG meetings and ICH M4Q(R2) Step 4.
  2025 and after: Forming an implementation WG to provide training and monitor the implementation of M4Q(R2).

- *What special actions to advance the topic through ICH, e.g. stakeholder engagement or training, can be anticipated either in the development of the guideline or for its implementation?*

  The following are potential special actions that may be taken to advance development of the guideline:

  - Presentations at major technical conferences to promote engagement on the ICH guideline during the consultation phase.
  - Example case studies and other information can be collected to help discussion at EWG.

  The following are potential special actions that may be taken to advance or promote implementation of the guideline:

  - Formal training materials related to the M4Q(R2) guideline can be created and distributed at inter-agency engagement activities and ICH-supported technical

workshops.
- Example case studies can be collected to form the basis of training materials of the guidelines when implemented.

3. <u>The impacts of the project</u>

- *What are the likely benefits (social, health and financial) to our key stakeholders of the fulfilment of the objective?*

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

  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.

- *What are the regulatory implications of the proposed work – is the topic feasible (implementable) from a regulatory standpoint?*

  M4Q(R2) guideline would be in alignment with ICH quality guidelines, and encourage regulatory convergence. The implementation of M4Q(R2) may require the revision of legislation in some regions. It may also require ICH to update some other quality guidelines.

- *Will the guideline have implications for the submission of content in the CTD/eCTD? If so, how will the working group address submission of content in the dossier? Will a consult be requested with the ICH M8 working group?*

  ICH M4Q(R2) describes the organization and content of CTD/eCTD. It will lay the foundation for the future ICH guideline on electronic data standard to support structured application. Therefore, a consult may be requested with the ICH M8 working group.

4. <u>Post-hoc evaluation</u>

- *How and when will the results of the work be evaluated?*

  The benefits of the M4Q(R2) CTD on Quality would be realized immediately from the issuance. In addition to obvious benefits in terms of presenting and assessing quality information in drug product submissions, the revised CTD would streamline capturing and assessing information as recommended by ICH Q8-Q14 and lay the foundation for structured applications.