令和3年12月22日
第44回　ICH即時報告会

ICH M4Q(R2) informal WG:「コモン・テクニカル・ドキュメント―品質に関する文書の作成要領に関するガイドライン」の改定

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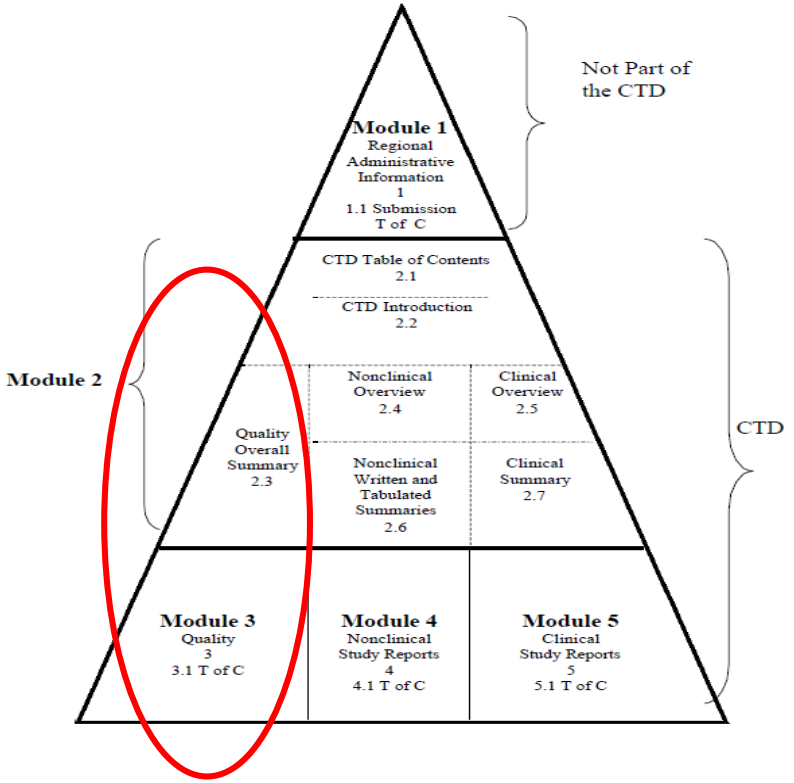
本発表は演者の個人的見解を含むものであり、PMDA及びICH M4Q（R2）の公式な見解ではないことにご留意ください。

本日の内容

- 背景
- 管理委員会で了承されたConcept Paper / Business Planの概要
- 今後の予定

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**
- M4Q(R1) was developed in 2002
- Major improvement over paper/local submission formats



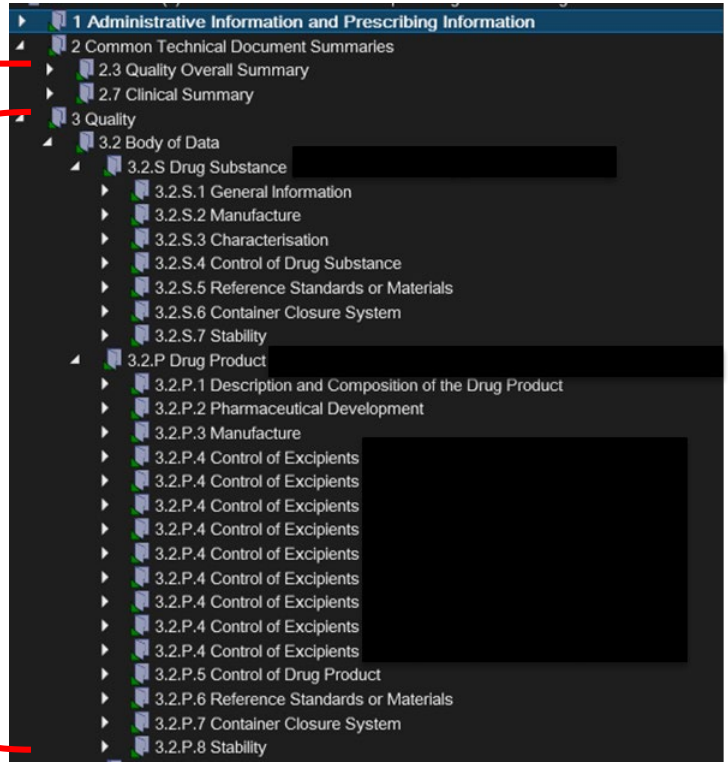
Current M4Q(R1) (from 2002)

- *Module 2 CTD Summaries*

includes summarization of information from Module 3 in the Quality Overall Summary (QOS)

- *Module 3 Quality*

Body of data displays quality data pertaining to drug substance and drug product manufacturing, analytical methods, process development, specification testing, reference standards, container closure system, and stability



ICH The Common Technical Document for the Registration of Pharmaceuticals for Human Use: Quality M4Q(R1) Quality overall Summary of Module 3, Module 3: Quality, September 2002
FDA Guidance for Industry M4Q: The CTD – Quality, August 2001

背景

- 2002年に調和合意されたM4Q(R1) は、20年近くの歳月の間、改訂が未実施。
- 2003年以降のICH Qトピックの成果であり「品質審査のパラダイムシフト」と言われるICH Q8以降のガイドラインとの整合は図られておらず、近年開発が進む複雑な製品（抗体薬物複合体、医薬品たるコンビネーション製品、組織加工製品）への対応、承認後変更管理への対応にも不十分。
- 品質審査の効率化が期待されるコンピューターサイエンスの発展に伴う各種デジタルツール（知識管理、クラウド申請、人工知能）の利活用に、現在のCTDは適切な様式とはなっていない。
- 2020年5月ICHアムステルダム会合で同時に新規トピックに採択された「Structured Product Quality Submissions（品質に関する申請資料の構造化、電子的なデータ標準化）」と相互に関係するものとされて、M4Q(R2)から着手

2021年11月バンクーバー会合までの活動

- 2021年8月、M4Q(R2) informal WG（iWG）を立ち上げ
- メンバーは、USFDA、EC、MHLW/PMDA、PhRMA、EFPIA、JPMAの他、ANVISA、Health Canada、NMPA(China)、TFDA、SFDA（Saudi Arabia）、GSCF、IFPMA、IGBAが含まれる。（オブザーバーとして 規制当局：CDSCO(India）、業界団体：APIC）
- 2021年9月からテレカンを実施し、ラポーターであるUSFDAが関係者との事前調整を進めていたthe outline of Concept Paperをたたき台にして、iWGでConcept Paperを検討
- 上記の検討の成果物であるConcept paperに沿って、過去のEWGにおける経験も踏まえたBusiness Planを作成

M4Q(R2)の進捗状況

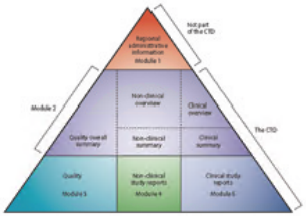
- 2020年5月, ICH 管理委員会でのM4Q(R2) の新トピック採択
- 2021年4月, ICH 管理委員会でのthe outline of Concept Paperの了承
- 2021年8月, ICH M4Q(R2) informal WGの設置
- 2021年11月, ICH 管理委員会でM4Q(R2) Concept Paper 、Business Plan の了承及びM4Q(R2) Expert WGの設置

2021年12月から月2回の頻度でテレカンを実施し、Work Planの作成及びStep1文書の骨子について議論が進行中

M4Q（R2）Concept Paper / Business Planの概要

Home \ ICH Standards \ CTD

CTD



The CTD Triangle

M4 : The Common Technical Document

The agreement to assemble all the Quality, Safety and Efficacy information in a common format (called CTD - Common Technical Document) has revolutionised the regulatory review processes, led to harmonised electronic submission that, in turn, enabled implementation of good review practices. For industries, it has eliminated the need to reformat the information for submission to the different ICH regulatory authorities.

The CTD is organised into five modules. Module 1 is region specific and Modules 2, 3, 4 and 5 are intended to be common for all regions. In July 2003, the CTD became the mandatory format for new drug applications in the EU and Japan, and the strongly recommended format of choice for NDAs submitted to FDA, United States.

More information: An electronic version of the Common Technical Document (eCTD) can be produced using the information developed by the eCTD Implementation Working Group.

M4: Organisation

M4Q: Quality

- **M4Q(R1) CTD on Quality**
- **M4Q Q&As (R1) Questions & Answers: CTD on Quality**
- **M4Q(R2) informal WG Revision of M4Q(R1)**

The M4Q(R2) informal WG is working on its Concept Paper and Business Plan.

Endorsed Documents

M4Q(R2) Concept Paper

M4Q(R2) Business Plan

Expert list

What Are Perceived Problems／現行の問題点①

- 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. **（各地地域での不十分なガイドラインの実装／施行状況）**

  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). **（品質審査のパラダイムシフトとの未整合）**

What Are Perceived Problems／現行の問題点②

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.（**複雑な製品に対応した様式が想定されていない**）

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.（**デジタル化を想定した様式となっていない**）

What Are the Issues to be Resolved?/ 解決策①

- 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. （対象製品の拡大）

What Are the Issues to be Resolved?/ 解決策②

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.（**承認後の変更管理ツールや**PQS/GMP**関連情報の**CTD**格納**）

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.（**革新的なデジタルツールにも適したCTD様式の最適化**）

What Are the Issues to be Resolved?/ 解決策③

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. **（現行のガイドライン、他の基準との整合、既存製品での知識の活用）**

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.**（開発の経緯、管理戦略の記載場所の改善）**

What Are the Issues to be Resolved?/ 解決策④

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. （CTD M2.3の充実化）

M4Q(R2) Objectives / 目的

- 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.

M4Q(R2) Importance ／改定の重要性・メリット

M4Q(R2) guideline would speed up patients and consumers' access to pharmaceuticals

- 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.

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.

M4Q(R2) guideline would be of great benefit to regulators.

- 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.

今後の予定

年	マイルストーン
2021	✓ コンセプトペーパーとビジネスプランの作成
2022	• 対面会合の実施 及びStep 1到達
2023	• 対面会合の実施 及びStep 2～Step 3（パブコメ）到達
2024	• 対面会合の実施 及びStep 4合意
2025 and after	• implementation WG を設置し、トレーニングの提供と各地域での実装（施行）状況のモニタリングの実施