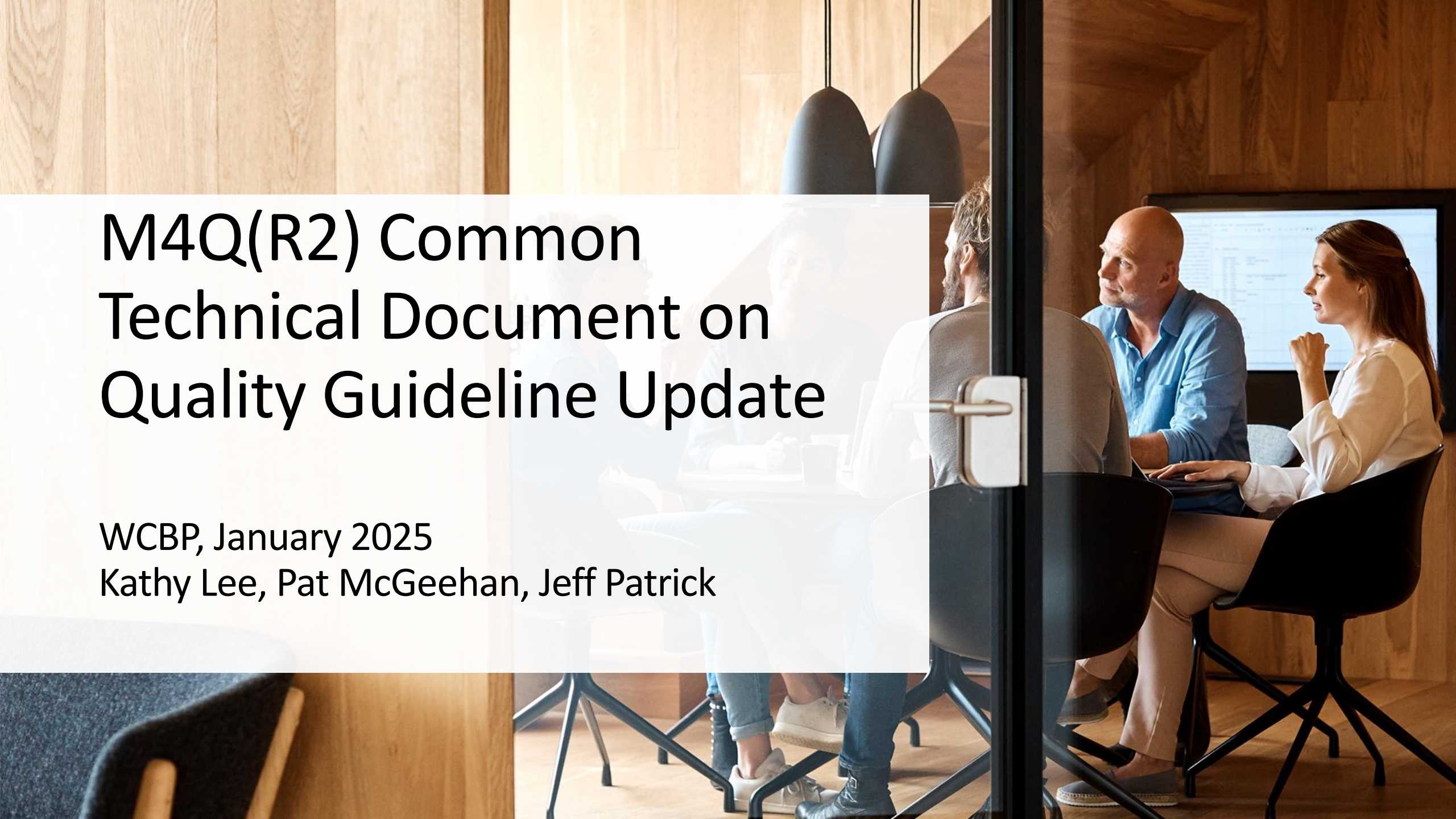


M4Q(R2) Common Technical Document on Quality Guideline Update

WCBP, January 2025

Kathy Lee, Pat McGeehan, Jeff Patrick

Overview of Topic

- The M4Q(R1) guidelines introduced in 2002 harmonized the format of quality information for the registration of pharmaceuticals for human use and offered great benefits to both industry and regulators.
- M4Q(R1) is due for revision to improve registration and lifecycle management efficiency, leverage digital technologies, and accelerate patient and consumer access to pharmaceuticals.

Why Upgrade Guidance?

Issues to be resolved

- Expand eCTD to include complex products and new therapeutic modalities inc. ADCs, vaccines, ATMPs/CGT
- Better align with modern quality guidelines Q8-Q14 that have been developed since ICH M4Q(R1)
- Leverage emerging tools & concepts inc. Adv. Mfg., CM, data tools, bioinformatics, etc.
- Better use of prior knowledge and risk-based principles
- Improved efficiency and effectiveness of regulatory submission and assessment
- Global harmonisation of CMC information in dossier
- Prepare for structured data submission in near future

Scope of M4Q

Location and structure of Quality Information

Enables Structured Data and Cloud Submissions

For both Initial Marketing Authorizations and Post-Approval Submissions

Ideally enables a single global submission

Does not “raise the bar” for quality information

Organization

Designed to be Flexible

Module 2.3

- Basis of regulatory assessment
- Facilitates Lifecycle Management
- Includes:
  - Introduction
  - Overall development
  - Control strategy
  - Core Quality Information
- Supports a risk-based regulatory assessment
  - Development Summary and Justifications
- Science and risk-based approach

Organization

Sections across Module 2.3 and Module 3

- Drug Substances (DS),
- Substance Intermediates (SI),
- Raw Materials (RM),
- Starting Materials (SM),
- Reference Standards/Materials (RS),
- Excipients (EX),
- Impurities (IM),
- Drug Products (DP),
- Product Intermediates (PI),
- Medical Devices (MD)

Organization

Each Section is organized into DMCS Model

- **D**escription: Identifies the material and its key characteristics.
- **M**anufacture: Outlines the production process.
- **C**ontrol: Describes quality control measures such as specifications.
- **S**torage: Container closure system, storage condition, stability, and retest period/shelf life

Relationships between Module 2 Core Quality Information, Development Summary and Justifications, and Module 3 Body of Data

	2.3.3 Core Quality Information	**2.3.4 Development Summary and Justification**	**3.2 Body of Data**
	Information related to what the material is and its key characteristics, which is considered necessary to enable marketing authorization and facilitate lifecycle management.	*Scientific and risk-based development summary and justifications related to what the material is and its key characteristics.*	*Supportive information including reports and data related to what the material is and its key characteristics.*
Description	Nomenclature, structure, composition, key characteristics	Characterization summary, formulation development and justification	Characterization data, formulation and justification data
Manufacture	Manufacturing process description, IPCs, critical process parameters	Process development and evaluation summary	Process development and evaluation data
Control	Specifications	Summary of batch analysis, justification of specifications	Batch analysis and justification data
Storage	Container closure system description, storage conditions, and retest period/shelf life	Summary of stability studies, justification of proposed container closure system	Container closure selection data, stability data

Organization

New term for “Combination Products”

Additional Sections in Module 2.3 in Core Quality Information

- Packaged Medicinal Products for **multiconstituent** products
- Pharmaceutical Product after transformation
- Analytical Procedures
- Facilities

Organization

Additional Sections in Module 2.3 Development and Justifications

- Integrated Development and Justifications, if applicable
  - Overview of comparability during development
- Integrated Discussion
  - Integrated justifications of extractables and leachables, if applicable
  - Integrated justifications of control of adventitious agents, if applicable
  - Development and justifications for products without a defined and/or isolated drug substance
    - Continuous manufacturing
    - ATMP
  - Integrated justifications of specific items, if applicable (Optional)
    - Justify commercial manufacturing process and control strategy

Organization

Additional Sections in Module 2.3 Development and Justifications

- Comparability and similarity with a reference product
  - Summary and Justifications of analytical and in vitro comparability with a reference product (generics and biosimilars), if applicable
  - Summary and Justifications of sameness with a product approved in a reference country if a reliance procedure is used

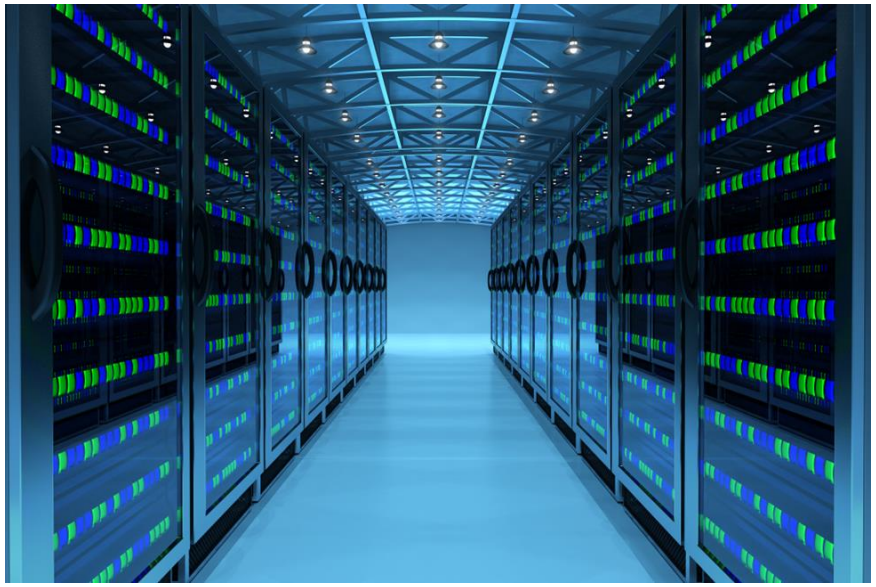
Organization

Additional Sections in Module 2.3 Product Lifecycle Management

- Listing Established Conditions (Optional)
- Reporting Categories for Making Changes to Established Conditions (Optional)
- Post-Approval Change Management Protocols (Optional)
- Post-Approval CMC Commitments, if Applicable

- **Change Summary and Justification**
  - Post Approval Changes
    - Summary of change
    - Proposed update to CQIs and/or DSJ or Module 3
    - Justification for changes

ICH M4Q(R2) Expert Working Group



Thank You!