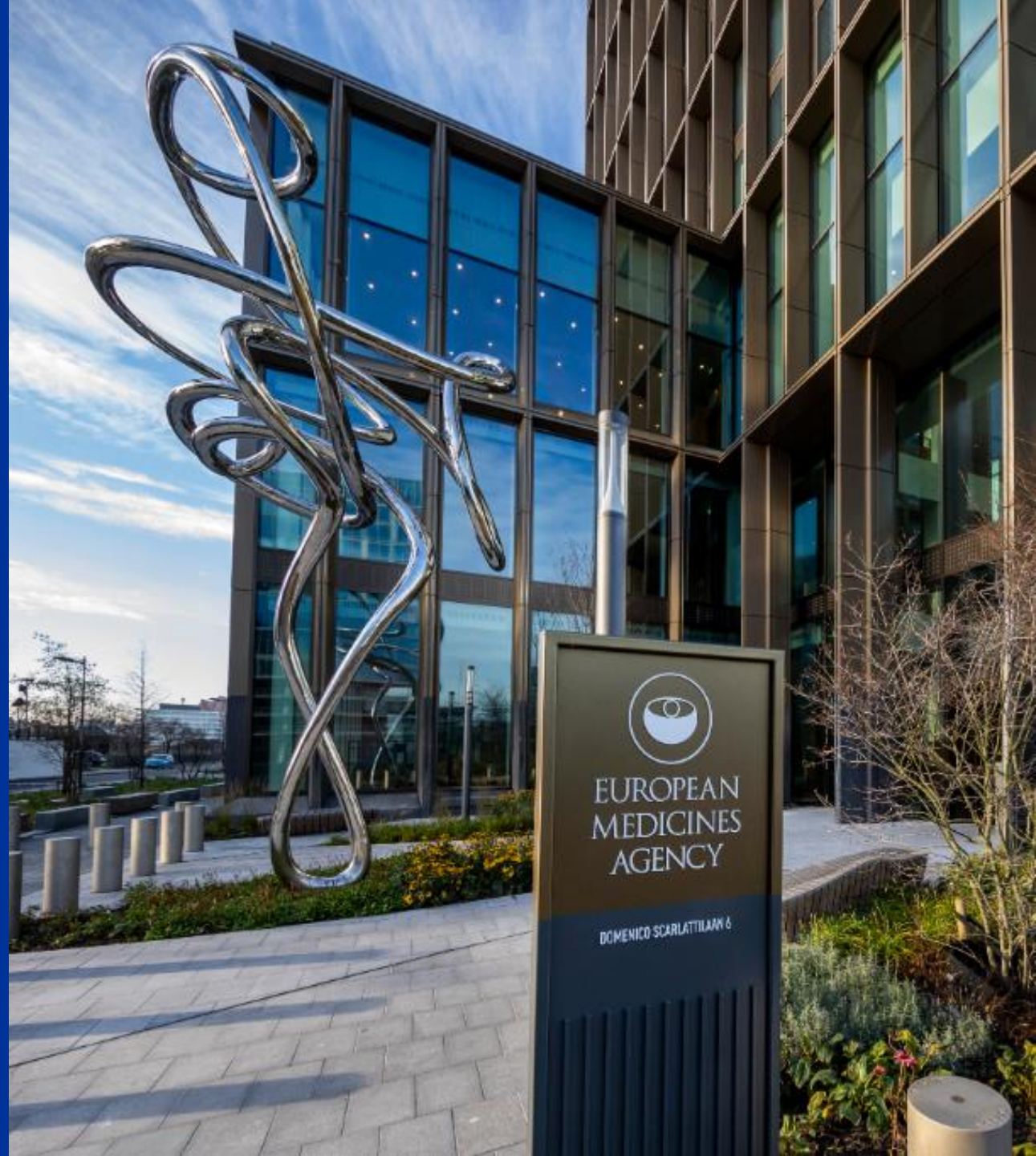
EMA
EUROPEAN MEDICINES AGENCY

ICH M4Q(R2) Revision overview and regulatory perspectives

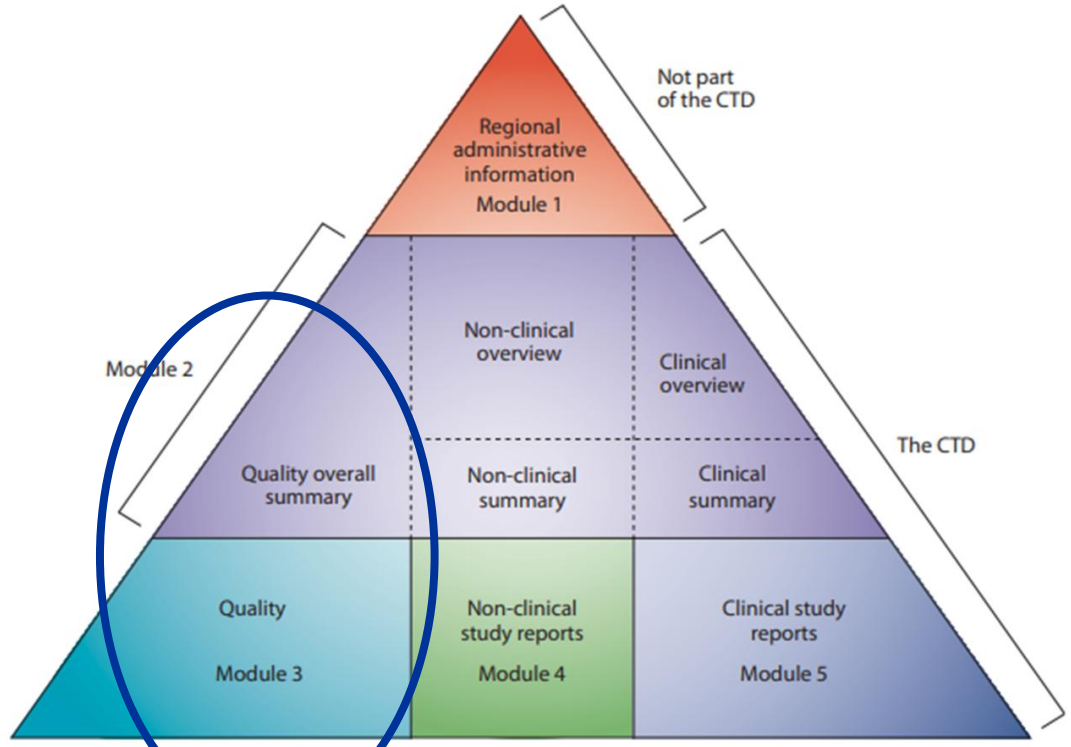
CASSS CMC Strategy Forum, 20-22 October 2025



What was M4Q designed to do?

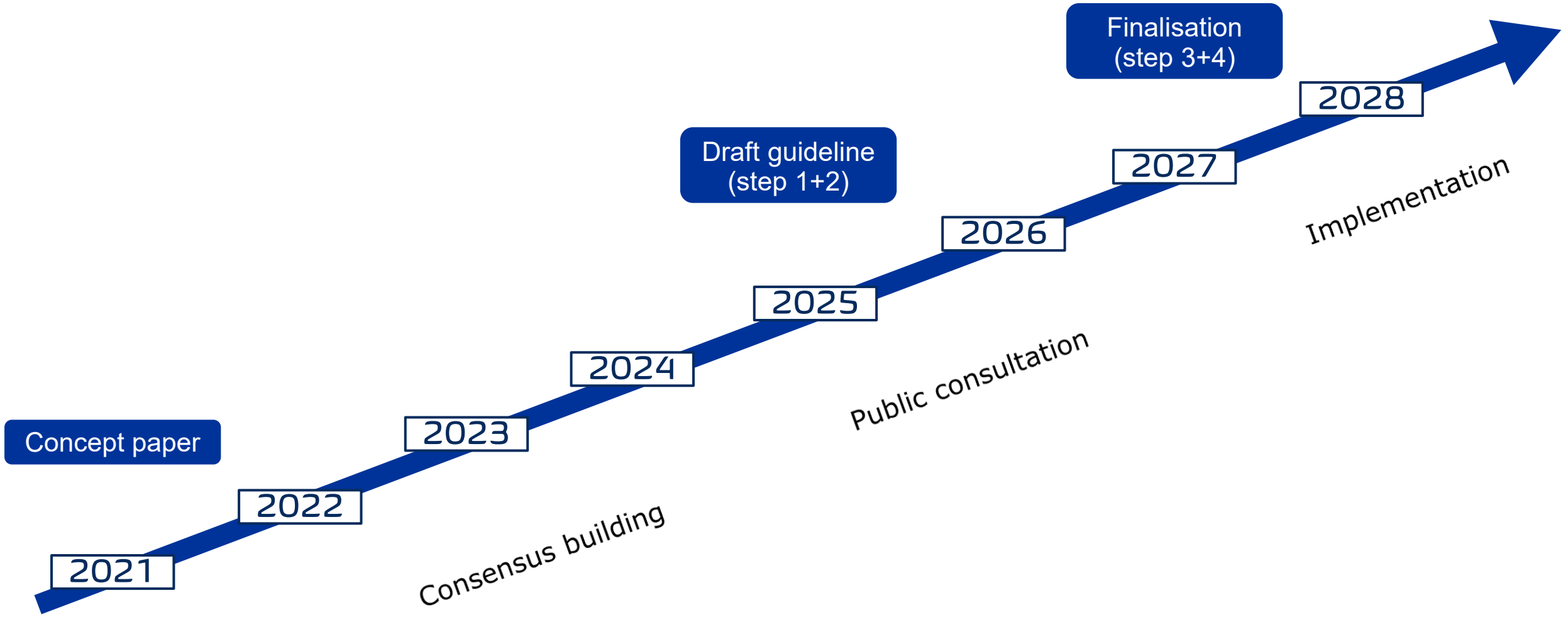
- Globally harmonized content and organization of quality information in Common Technical Document (CTD)/eCTD
  - **Module 2.3 Quality Overall Summary (QOS)**
  - **Module 3 Quality**

- M4Q was a substantial improvement compared to the prior state with regional submission formats



The CTD triangle. The Common Technical Document is organized into five modules. Module 1 is region specific and modules 2, 3, 4 and 5 are intended to be common for all regions.

ICH M4Q(R2) roadmap



Current revision of M4Q

INTERNATIONAL COUNCIL FOR HARMONISATION OF TECHNICAL REQUIREMENTS FOR PHARMACEUTICALS FOR HUMAN USE

ICH HARMONISED GUIDELINE

THE COMMON TECHNICAL DOCUMENT FOR THE REGISTRATION OF PHARMACEUTICALS FOR HUMAN USE: QUALITY M4Q(R2)

Draft version
Endorsed on 14 May 2025
Currently under public consultation

M4Q(R2) Objectives

Expand the scope of M4Q(R1) guideline to include all pharmaceutical drug substances and products (both chemical and biological)

Establish the role of M4Q(R2) as the main source of the structure and location of regulatory quality information.

Organize product and manufacturing information in a suitable format for easy access, analysis, and knowledge management.

Incorporate concepts and data expectations presented in ICH Quality guidelines and aligning with currently recognized international standards and guidelines.

Better capture the pharmaceutical development and the proposed overall control strategy, which should be the backbone of the revised M4Q structure.

Enhance the Quality Module 2 to facilitate the efficiency and effectiveness of regulatory submissions and assessments.

[ICH M4Q-R2 Concept paper]

ICH's Effort to Shape the Future

STEP 1

ICH M4Q(R2) defines the new structure of Module 2.3 and Module 3

STEP 2

SPQS (M16) will define Structured Product Quality Submissions

Cloud computing

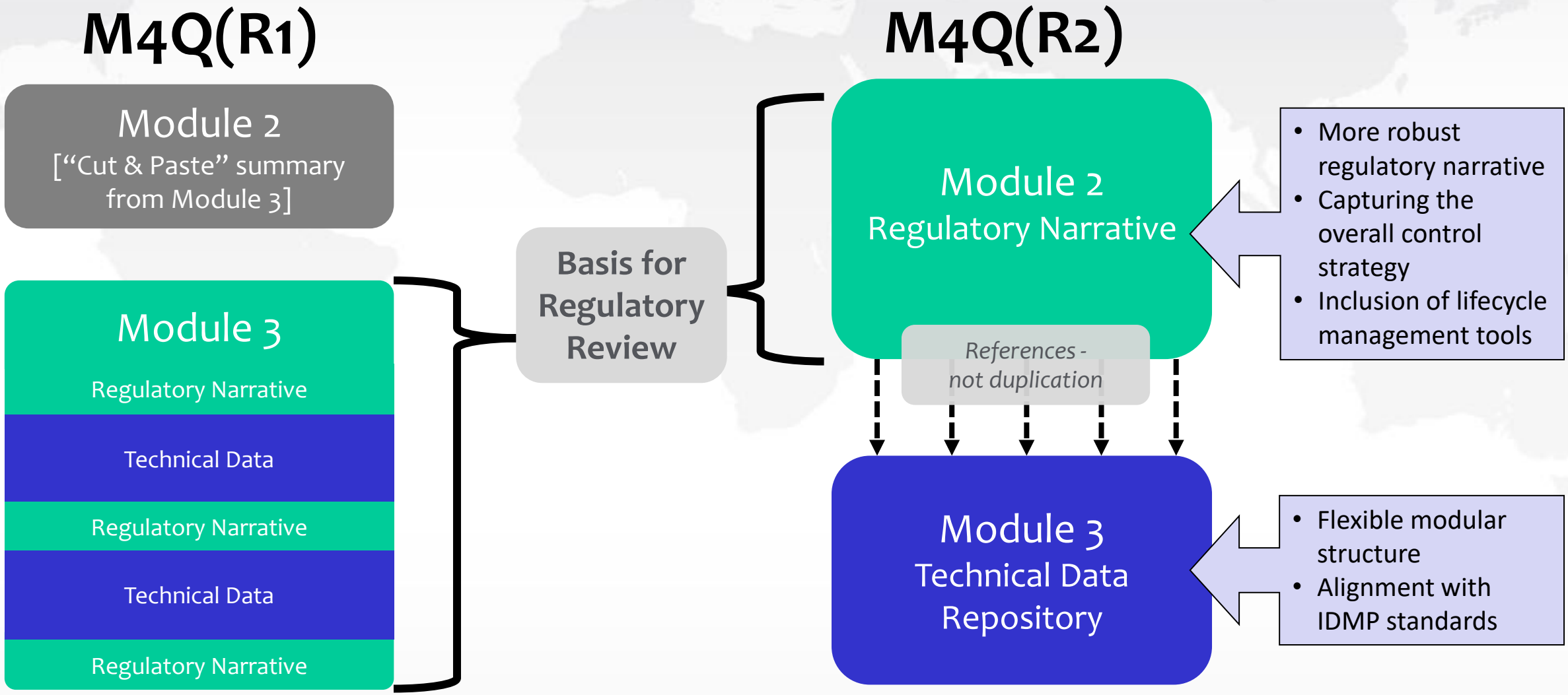
Big data analytics

Knowledge management

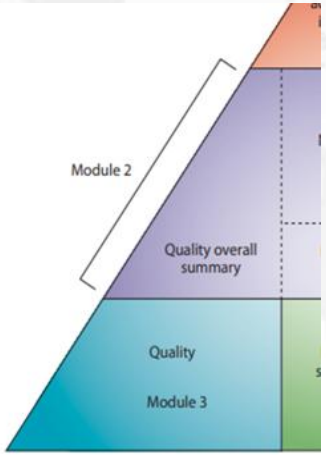
Artificial Intelligence

Revision overview

Changes to the location of information, regulatory expectations are not changing



M4Q(R2) Structure Overview



Module 2

2.3.1 General Information

Essential product details, optionally supported by a schematic

2.3.2 Overall Development and Overall Control Strategy

High level summary of the **development and integrated control strategy**, including the QTPP, CQAs, and how control elements ensure **consistent quality**

2.3.3 Core Quality Information (CQI)

Information needed to support a science- and risk-based **review for product approval** and ongoing **lifecycle management**.

2.3.4 Development summary and Justification (DSJ)

Scientific and risk-based rationale for development, including **justifications for specifications and control strategies**

2.3.5 Product Lifecycle Management

Strategy for managing **post-approval changes**, including a summary of changes, the PLCM, and any associated protocols or commitments

2.3.6 Product Quality Benefit Risk (Optional)

Optional summary of **how quality-related risks are mitigated and justified in the context of the product's therapeutic benefits**, especially relevant for expedited review pathways

Module 3

3.2 Body of Data

Detailed descriptions of methods, **data**, and other relevant quality information that supports Module 2.3

M4Q(R2) introduces specific subsections for materials/components

- Facilitates re-use of information/ minimises duplication
- Alignment with ISO IDMP standards
- Information organised in defined substructure (DMCS)

- Information on analytical procedures and facilities applies across materials and is presented in dedicated sections with separate substructure


Product Intermediate (PI)


Drug Substance (DS)


Substance Intermediate (SI)


Packaged Medicinal Product *for multiconstituent products* (PM)


Pharmaceutical Product *after transformation* (PH)


Medical Device (MD)


Raw Material (RM)


Starting / Source Material (SM)


Excipient (EX)


Reference Material (RS)


Impurities (IM)

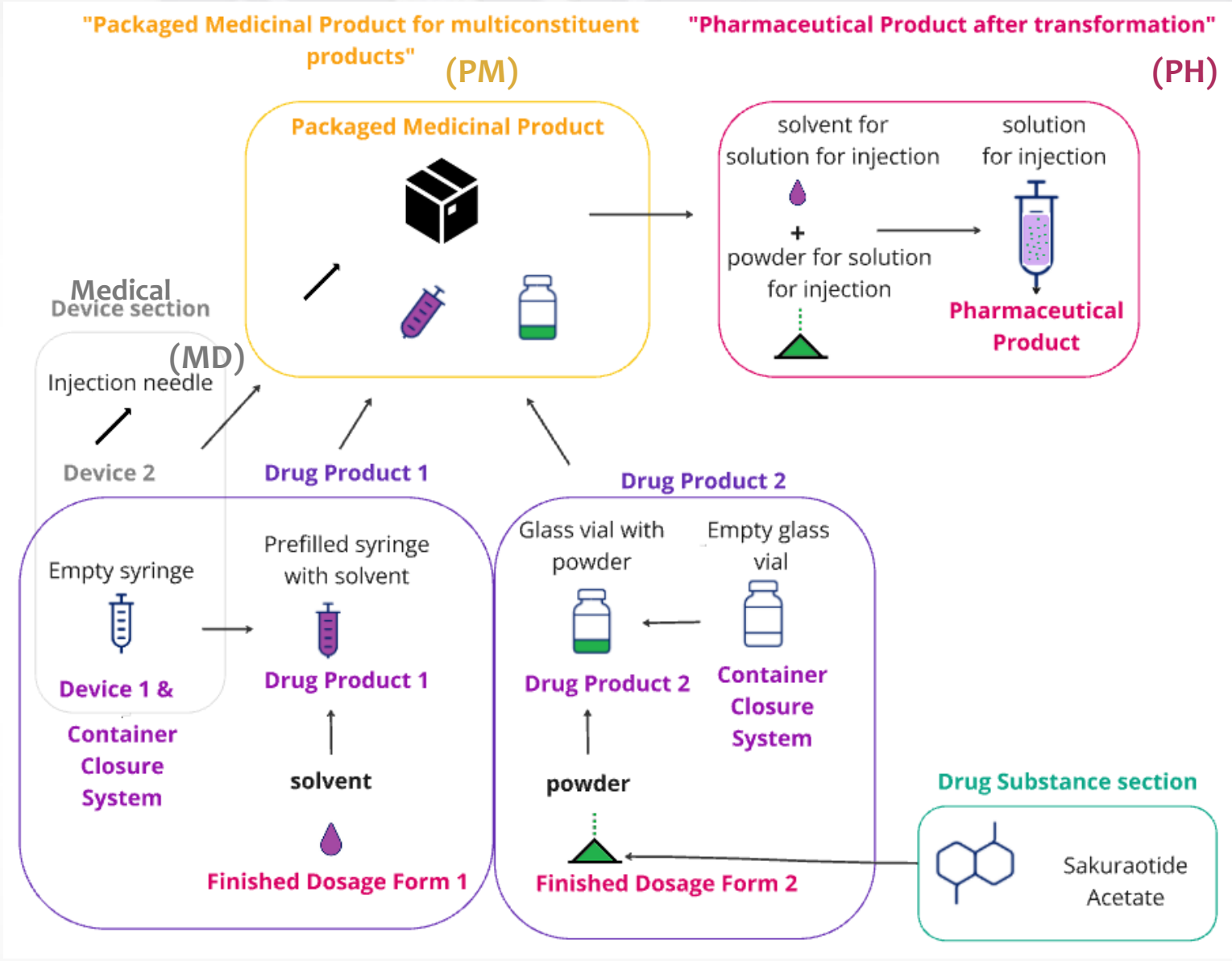

Drug Product (DP)


Facilities


Analytical Procedures

Illustration for explanation of DP, PM, PH, MD

- **DP1** PFS (prefilled syringe)
- **DP2** Powder in glass vial
- **PM section:** information about the packaging configuration/ packaging process/ packaging material as necessary and applicable: needles + PFS + powder for solution for injection
- **PH section:** description of the preparation of the solution for injection (transformation of the powder in glass vial to the solution for injection), compatibility studies, in-use stability as applicable
- **MD section:** information about empty devices (syringe and injection needle) in accordance with regional requirements



M4Q(R2) Organization – Standard Subsections

Most subsections of M4Q(R2) follow a standardized Description, Manufacture, Control, Storage (DMCS) model for information about materials, such as substances and products

D	Description	Identifies the material and its key characteristics
M	Manufacture	Outlines the production process
C	Control	Describes quality control measures such as specifications
S	Storage	Provides stability, container closure information, and retest period/self-life

This DMCS model applies across the main dossier sections to support efficient information management and retrieval

Example of DMCS Model for Drug Product

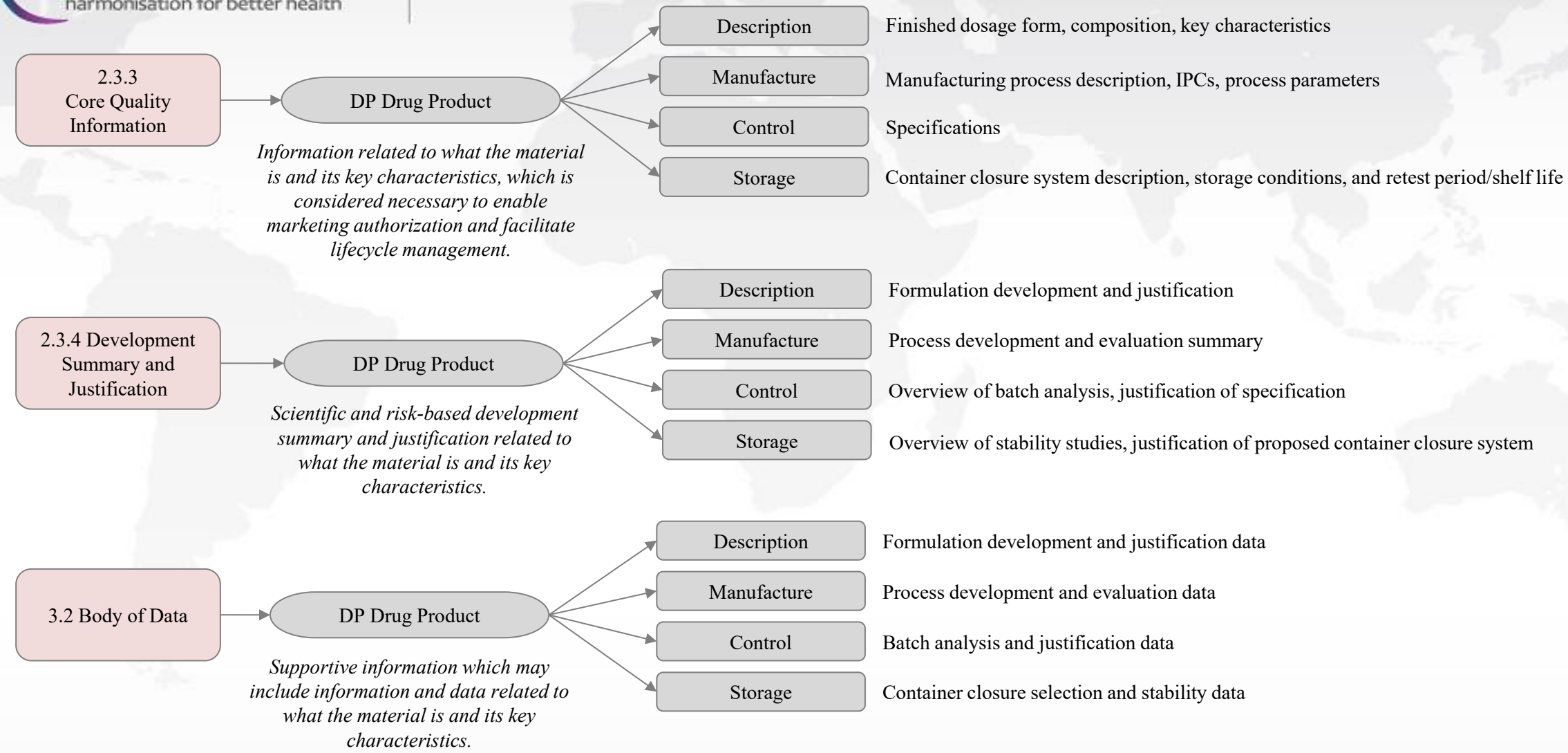
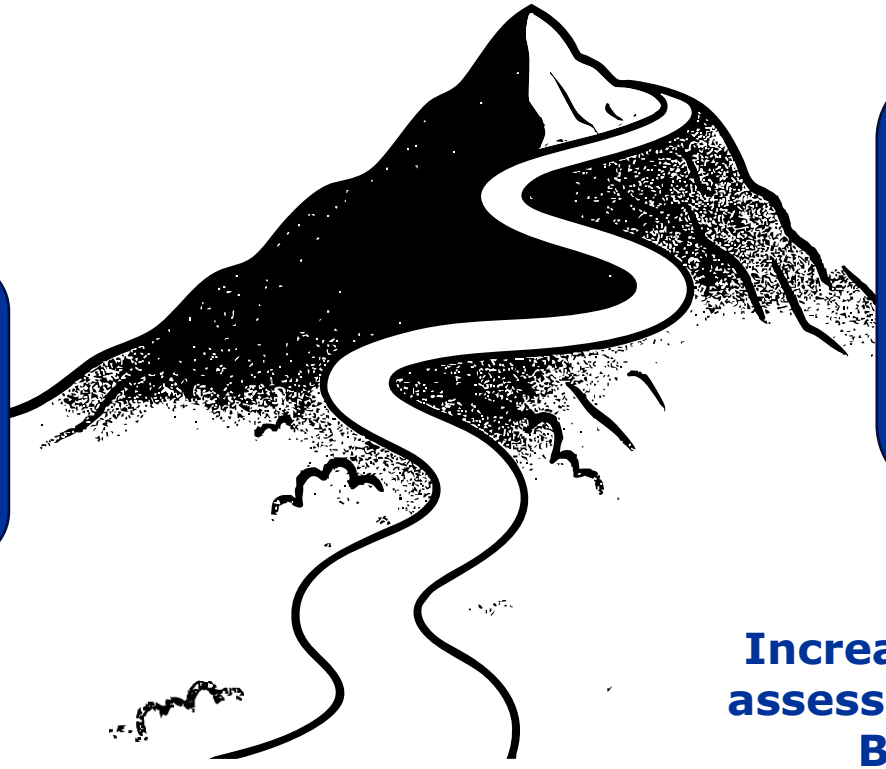


Figure 1: Illustration of relationships among sections 2.3.3 Core Quality Information, 2.3.4 Development Summary and Justifications, and Module 3.2 Body of Data in the context of DMCS Model used for materials.

Regulatory perspectives

…M4Q(R2) will combine innovation, efficiency, and global harmonization to help patients receive treatments faster.

Complex change management
- Legislation update
- Training
- Revision of guidance
- New assessment templates
- New/updated IT tools



Benefits
- Streamlined regulatory assessment
- Efficient data analysis/automation
- Improved product oversight (including lifecycle)
- Improved consistency in regulatory decision making
- Improved communication with stakeholders

The uphill stage of implementation will be challenging…

Increased efficiency in assessment & enhanced B/R decisions

→ Improve patients' access to high quality medicines

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Useful Links

ICH M4Q(R2) Draft Guideline:

https://database.ich.org/sites/default/files/ICH%20M4Q%28R2%29_Draft_Guideline_2025_0514.docx

ICH M4Q(R2) Concept Paper:

https://database.ich.org/sites/default/files/ICH_M4Q-R2_ConceptPaper_Endorsed_2021_1115.pdf

ICH Public Consultations webpage:

https://www.ich.org/page/public-consultations

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Thank you

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