ICH M4Q(R2)

Quality CTD (Common Technical Document)

ASPHALION
Knowledge from experience

25 years

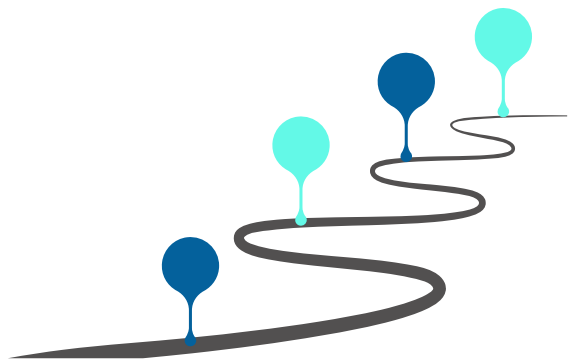
Scope

- All **pharmaceutical DS & DP** (chemical and biological)
- Incl. antibody-drug conjugates, vaccines, ATMPs, cell & gene therapies, tissue engineered products or combination products

Purposes

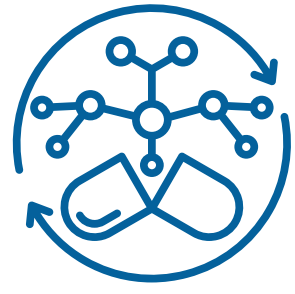
- Explaining and defining the **organization of CMC info. for Modules 2 and 3**
- Laying the foundation for **electronic data standards to support structured applications**
- Alignment with other **ICH Guidelines (ICH Q8 to Q14)**
- Encouraging **risk-based approaches** (QTPP, TRA, PCS)

Timelines



- Under public consultation since May 14th, 25
- Step 4 is expected by June 2027
- Early adoption is not expected till 2028
- Implementation will be linked to eCTD 4.0
- Implementation may trigger regional and additional ICH guidelines updated

Organizational Levels



1. Component Roles

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

2. DMCS

- **D.Description**: Identifies the material and its key characteristics
- **M.Manufacture**: Outlines the production process and process controls
- **C.Control**: Describes quality control measures such as specifications
- **S.Storage**: Provides container closure system, stability, storage condition, and retest period/shelf life

Example of DMCS Model for Drug Product

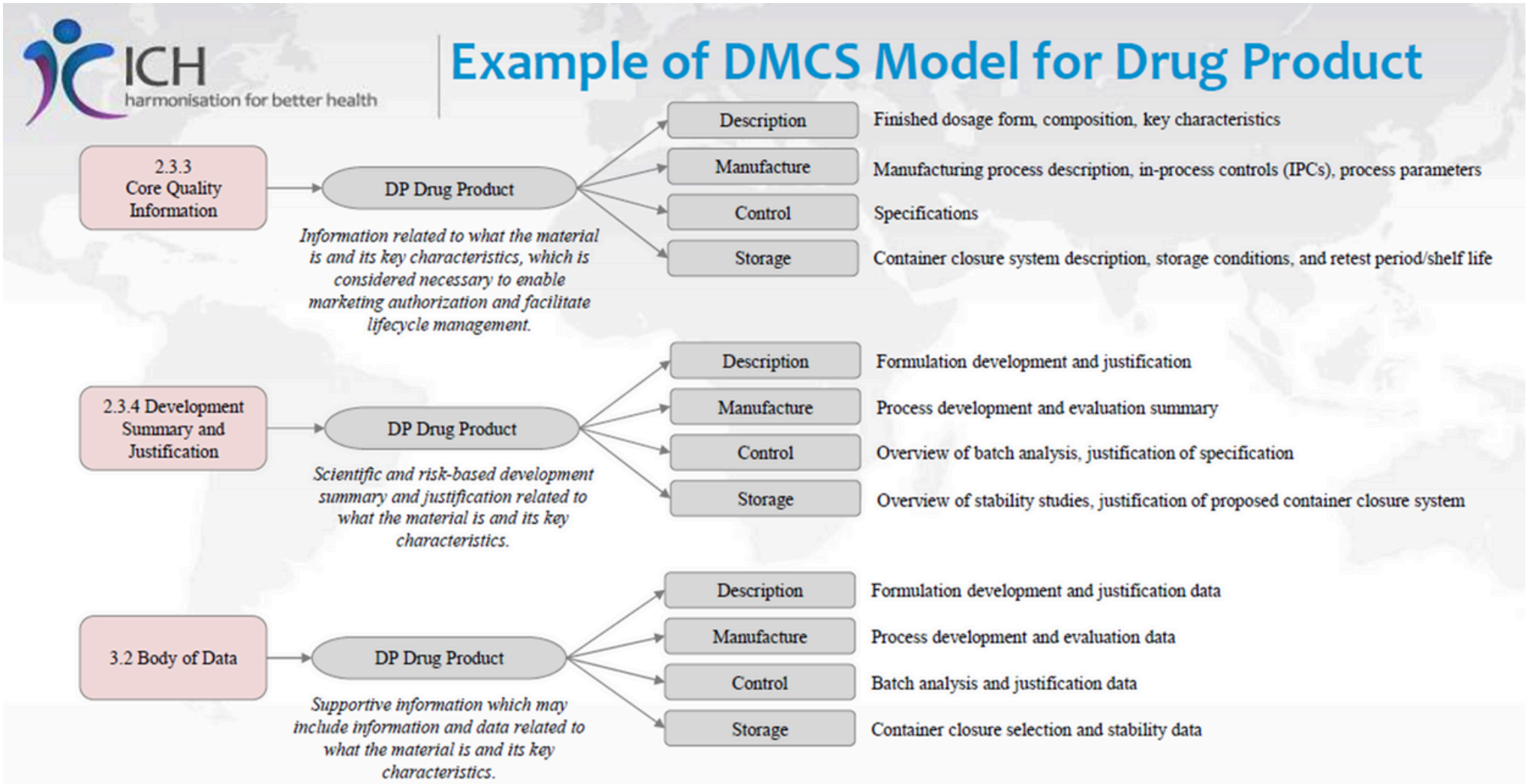
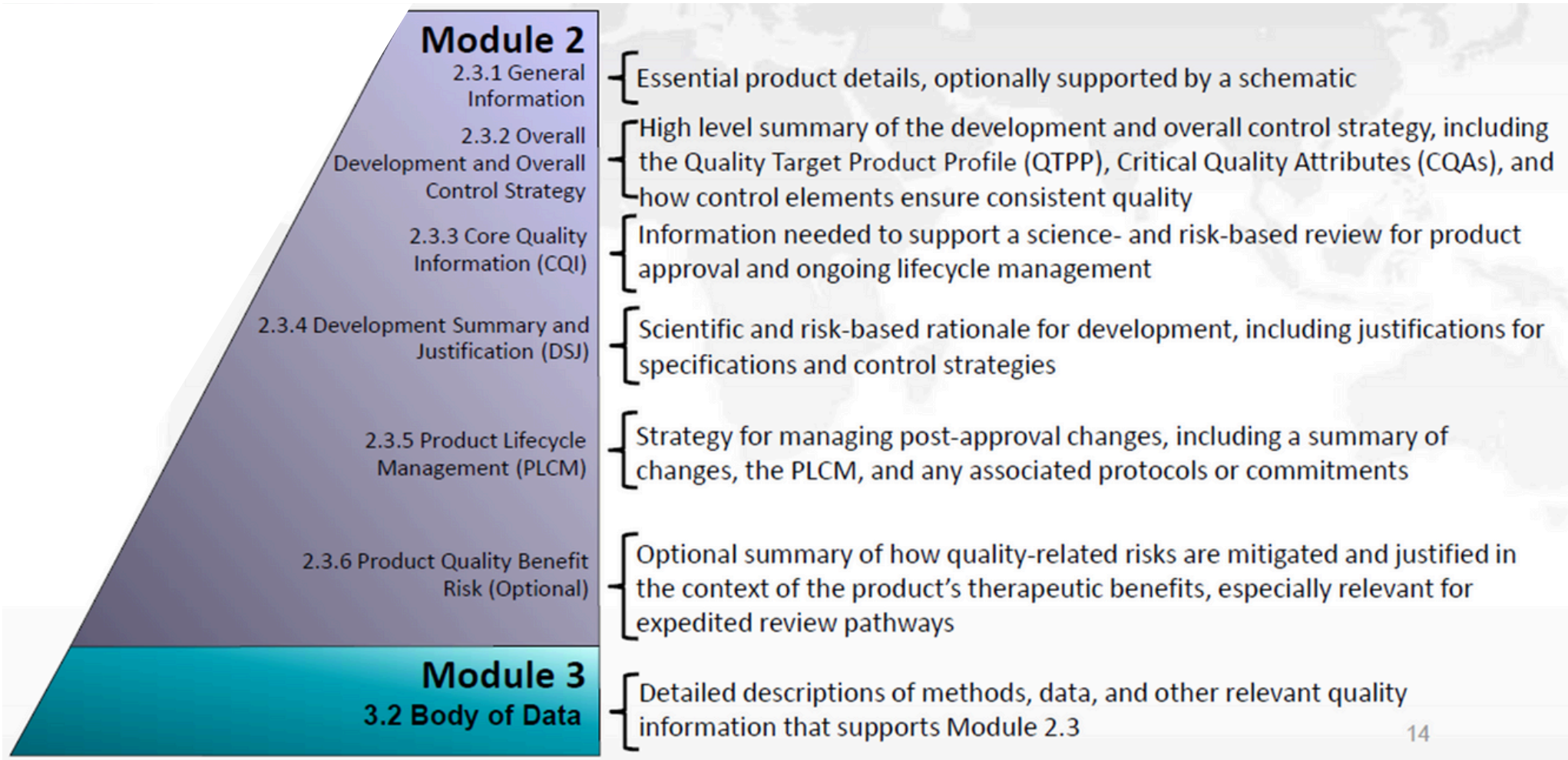
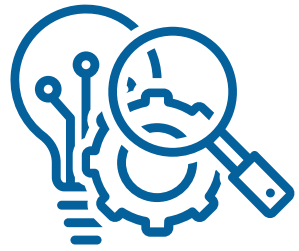


Figure 1: Illustration of relationships among sections 2.3.3 Core Quality Information, 2.3.4 Development Summary and Justifications, and Module 3.2 Body of Data in the context of DMCS Model used for materials.

Module 2 + 3


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 overall control strategy, including the Quality Target Product Profile (QTPP), Critical Quality Attributes (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 (PLCM)
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
14

Module 2



2.3.1 General Information

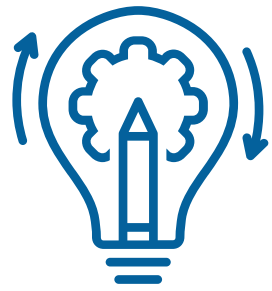
2.3.2 Overall Development and Overall Control Strategy

- 2.3.2.1 Quality Target Product Profile
  - 2.3.2.1.1 Critical Quality Attributes
- 2.3.2.2 Overall Product Development Strategy
- 2.3.2.3 Overall Control Strategy Representation

2.3.3 Core Quality Information

- 2.3.3.DS Drug Substances
- 2.3.3.SI Substance Intermediates
- 2.3.3.SM Starting/Source Materials
- 2.3.3.RM Raw Materials
- 2.3.3.EX Excipients
- 2.3.3.RS Reference Standards and/or Materials
- 2.3.3.DP Drug Products
- 2.3.3.PI Product Intermediates
- 2.3.3.MD Medical Devices
- 2.3.3.PM Packaged Medicinal Products for multiconstituent products
- 2.3.3.PH Pharmaceutical Product after transformation
- 2.3.3.AP Analytical Procedures
- 2.3.3.FA Facilities

Module 2



2.3.4 Development Summary and Justification

2.3.4.IN Integrated Development and Justifications

2.3.4.IN.1 Overview of changes during development

2.3.4.IN.2 Integrated discussions

2.3.4.IN.2.1 Integrated justifications of extractables and leachables

2.3.4.IN.2.2 Integrated justifications of control of adventitious agents

2.3.4.IN.2.3 Development and justifications for products without a defined and/or isolated drug substance

2.3.4.IN.2.4 Integrated justifications of specific items

2.3.4.IN.3 Equivalency, similarity or sameness with a reference product

2.3.4.IN.3.1 Summary and Justifications of analytical and in vitro similarity with a reference product

2.3.4.IN.3.2 Summary and Justifications of sameness with a product approved in a reference country

2.3.4.DS Drug Substances

2.3.4.SM Starting/Source Materials

2.3.4.RS Reference Standards and/or Materials

2.3.4.DP Drug Products

2.3.4.MD Medical Devices

2.3.4.PM Packaged Medicinal Products for multiconstituent products

2.3.4.PH Pharmaceutical Product after transformation

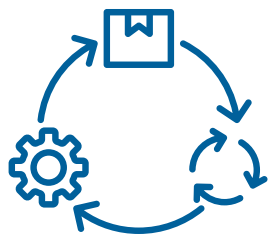
Module 2

2.3.4. AP Analytical Procedures

2.3.4.AP.1 Analytical Procedure Justification

2.3.4.AP.2 Analytical Procedure Validation/Qualification

2.3.4.AP.3 Analytical Procedure Development



2.3.5 Product Lifecycle Management

2.3.5.1 Change Summary and Justifications

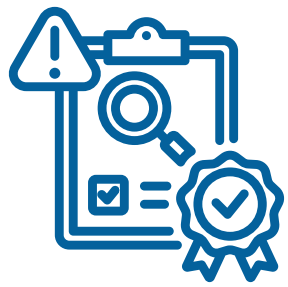
2.3.5.2 Product Life Cycle Management Document (PLCM)

2.3.5.2.1 List of Established Conditions and Reporting Categories

2.3.5.2.2 Post-approval Quality Commitments

2.3.5.2.3 List of Post-Approval Change Management Protocols

2.3.5.3 Content of Post-Approval Change Management Protocols



2.3.6 Product Quality Benefit Risk

Module 3

3.2.DS Drug Substances
3.2.SI Substance Intermediates
3.2.SM Starting/Source Materials
3.2.RM Raw Materials
3.2.EX Excipients
3.2.RS Reference Standards and/or Materials

3.2.IM Impurities
3.2.DP Drug Products
3.2.PI Product Intermediates
3.2.MD Medical Devices
3.2.PM Packaged Medicinal Products for multiconstituent products
3.2.PH Pharmaceutical Product after transformation
3.2.AP Analytical Procedures
- 3.2.AP.1 Analytical Procedure Description
- 3.2.AP.2 Analytical Procedure Validation/Qualification
- 3.2.AP.3 Analytical Procedure Development

3.2.FA Facilities

Metadata (I)

R: Required / **O**: Optional

Metadata	Module 2	Module 3
DS Name	233DS-234DS (O) 233RS/233RM/233SM-234SM/233SI (R)	32DS (O) 32RS/32RM/32SM/32SI (R)
DP Name	233DP-234DP (O) 233PI/233RS/233EX (R)	32DP (O) 32PI/32RS/32EX (R)
AP Name or Code (O)	233AP-234AP	32AP
RM Name	233RM (R)	32RM (O)
EX Name	233EX (R)	32EX (O)
RS Name	233RS (R)	32RS-234RS (O)
SM Name	233SM-234SM (R)	32SM (O)
MD Name (O)	233MD-234MD	32MD
PI Name (O)	233PI	32PI
IM Name (R)	233RM/233SM-234SM	--
SI Name (O)	233SI	32SI
PH Name (O)	233PH-234PH	32PH
PM Name (O)	233PM-234PM	32PM

Metadata (III)

Metadata	Module 2	Module 3
Manufacturer (R)	233FA/233PH-234PH/233PM-234PM/233MD-234MD/233PI/233EX/233RM/233SI/233DS-234DS/233DP-234DP/233RS-234RS	32FA/32PH/32PM/32MD/32PI/32EX/32RM/32SI/32DS/32DP/32RS
IM Substance Manufacturer (R)	--	32RM
Strenght (R)	233PH-234PH/233PM-234PM/233DP-234DP	32PH/32PM/32DP
Manufactured Dosage Form (R)	233DP-234DP	32DP
Combined Dosage Form (R)	233PM-234PM	32PM
Administered Dosage Form (R)	233PH-234PH	32PH
Purpose (R)	233AP-234AP	32AP
Material Type (R)	233AP-234AP	32AP

R: Required / **O**: Optional

Source: https://ich.org/page/ctd

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ASPHALION
Knowledge from experience

25 years