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CMC Strategy Forum Japan 2025

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ICH Q12 implementation in Japan, and current situation of ICH M4Q (R2)

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Disclosure

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The speaker is affiliated with Pharmaceuticals and Medical Devices Agency.

The views expressed in this presentation are those of the author and do not necessarily reflect the official views of Pharmaceuticals and Medical Devices Agency.

Abstract

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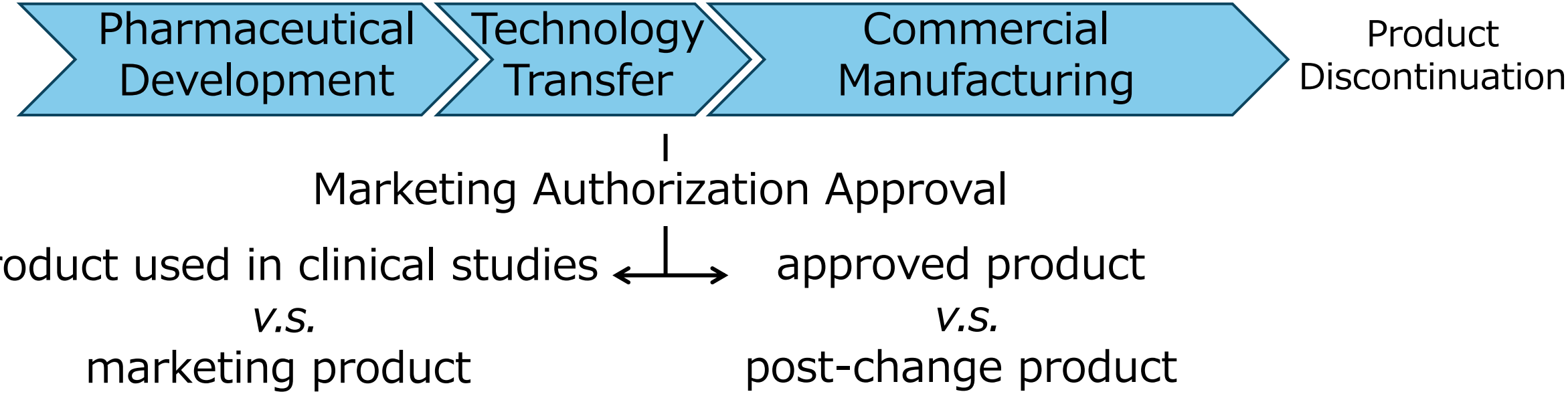
- Background
- ICH Q12 implementation in Japan
- Current situation of ICH M4Q (R2)
- Summary

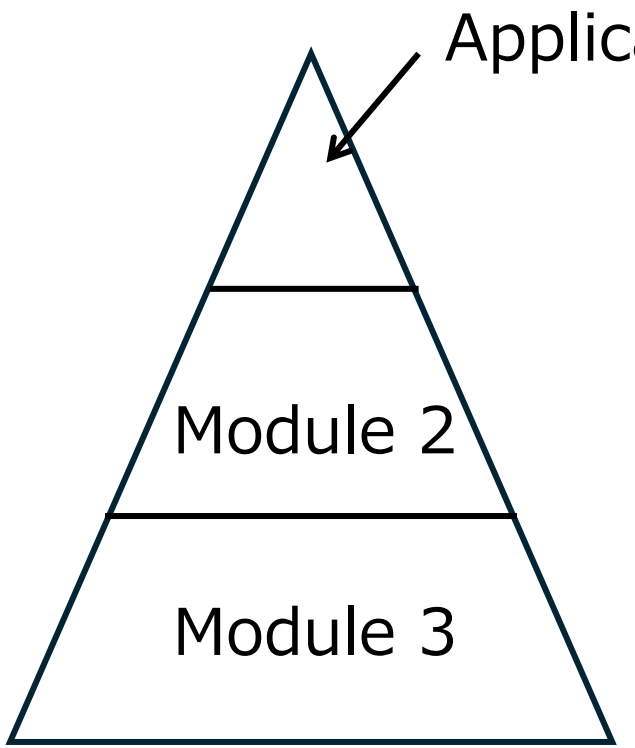
Background

Through product lifecycle,
comparability exercise must be conducted based on ICH Q5E.



Background

In Japan, Application form is required to maintain through lifecycle.



CTD

Approved matters

- Content
- Indication
- Specification
- Manufacturing process
- Storage condition and shelf life

etc.

To change approved matters, regulatory submission is required

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Overview of ICH Q12

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Core Guideline

1. Introduction
2. Categorisation of Post-Approval CMC Changes
3. Established Conditions (ECs)
4. Post-Approval Change Management Protocol (PACMP)
5. Product Lifecycle Management (PLCM) Document
6. Pharmaceutical Quality System and Change Management
7. Relationship Between Regulatory Assessment and Inspection
8. Structured Approaches for Frequent CMC Post-Approval Changes
9. Stability Data Approaches to Support the Evaluation of CMC Changes
10. Glossary
11. References

Established Conditions (ECs)

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ECs definition in ICH Q12

ECs are legally binding information considered necessary to assure product quality. As a consequence, any change to ECs necessitates a submission to the regulatory authority.

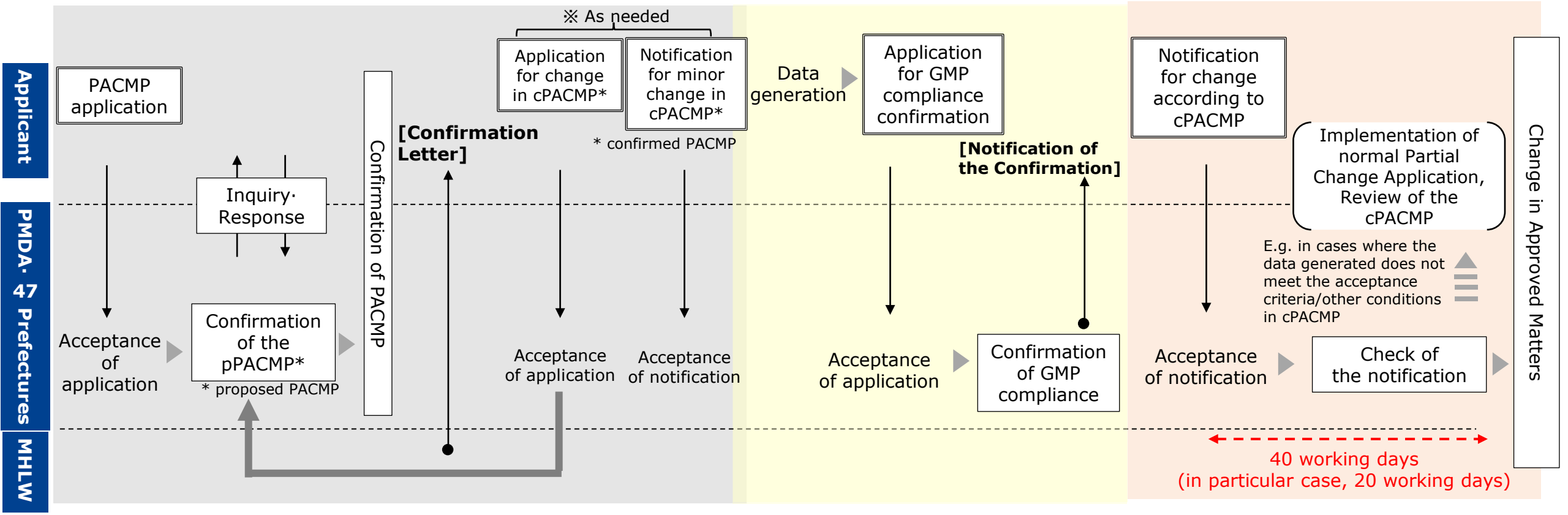
Example of description of manufacturing process in Application form.

> Step X: Production culture
> Medium and cell culture from expand culture are transferred into a XXX L bioreactor. Bioreactor temperature, pH and O2 are controlled within ○○ - ××℃, pH○○ - ××, and "○○ - ××"%. After ≪○○ days≫, the culture is harvested.

Approved matters in Application form seem to correspond to ECs. However, these approved matters are not necessarily identified in line with ICH Q12.

PACMP

Legislated PACMP was started from Aug. 2021 in Japan.



https://www.mhlw.go.jp/web/t_doc?dataId=00tc5989&dataType=1&pageNo=1 (in Japanese)

Product Lifecycle Management (PLCM) Document

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PLCM document definition in ICH Q12

The PLCM document outlines the specific plan for product lifecycle management that includes the ECs, reporting categories for changes to ECs, PACMP (if used) and any post-approval CMC commitments.

In Application form

- ECs
- Reporting categories for changes to ECs

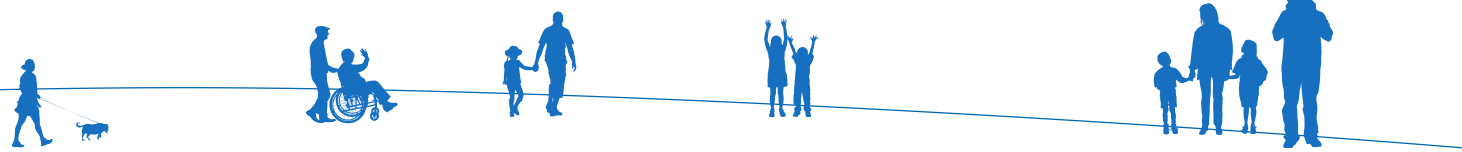
→ Approved matters are written with reporting categories.

- PACMP

→ PACMP application needs another application form, but it links to the marketing authorization application form.

- Post-approval CMC commitments

→ Application form includes post-approval CMC commitments.



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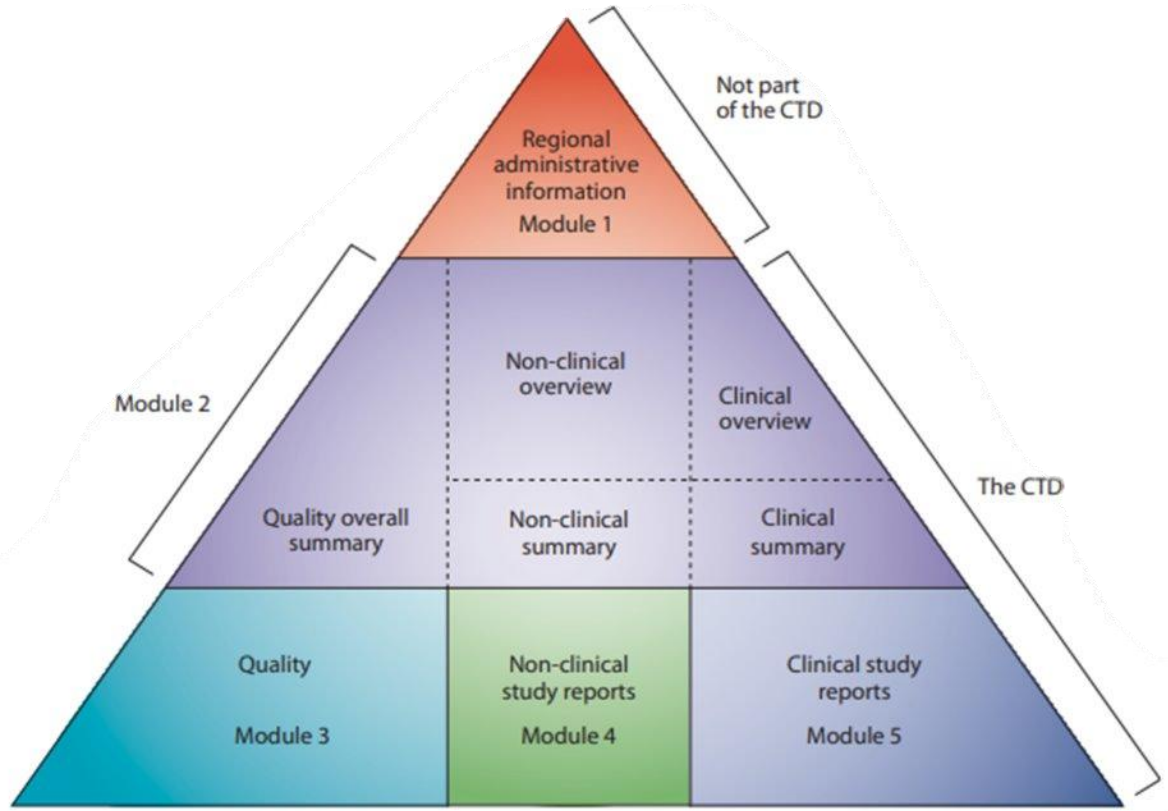
CTD M4Q (R1)

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

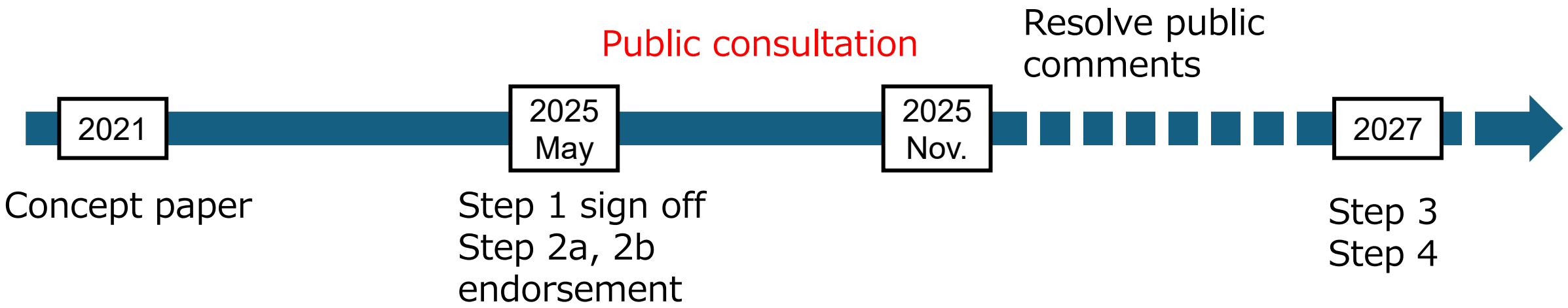
- M4Q(R1) was a substantial improvement compared to the prior state with regional submission formats



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 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

M4Q(R2) Road map



Current vs Future Framework

M4Q(R1)

Module 2
["Cut & Paste" summary from Module 3]

Module 3
- Regulatory Narrative
- Technical Data
- Regulatory Narrative
- Technical Data
- Regulatory Narrative

Basis for Regulatory Review

M4Q(R2)

Module 2
Regulatory Narrative

- More robust regulatory information
- Capturing the overall control strategy
- Inclusion of lifecycle management tools

References - not duplication

Module 3
Technical Data Repository

- Flexible modular structure
- Alignment with IDMP standards

Modified from presentation slide for public consultation
https://www.ich.org/page/ctd

M4Q (R2) Design

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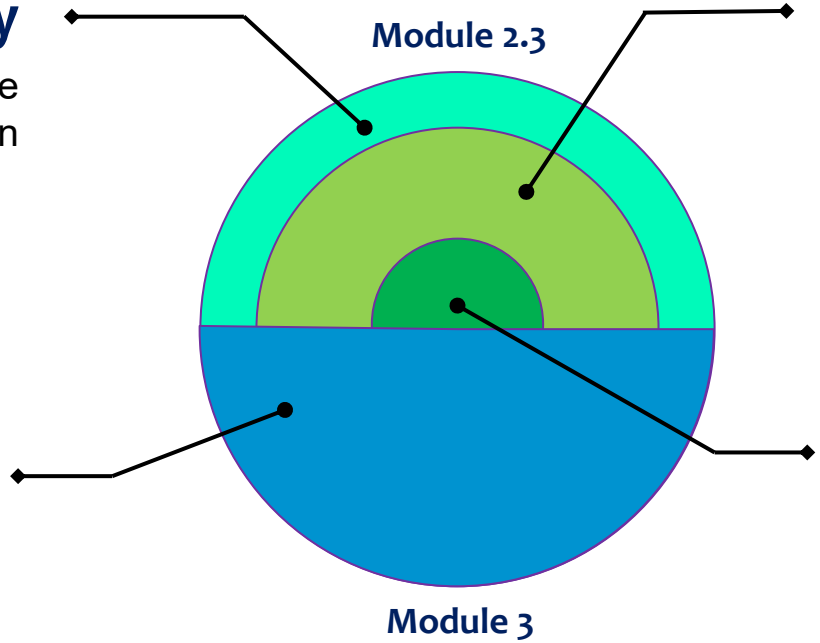
Overall Development and Overall Control Strategy

Provide a holistic view of the medicinal product and submission



Development Summary and Justifications

Summarizes the development process and provides justifications

Body of Data

Offers additional in-depth information to support the submission

Core Quality Information

Focuses on the essential quality aspects of the product

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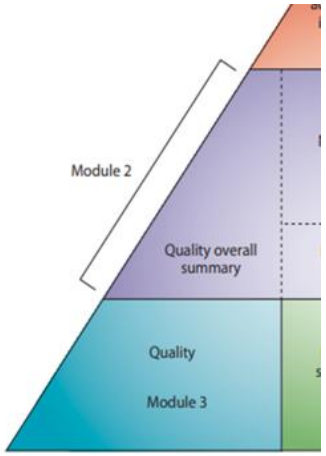
Structure of M4Q(R2)



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 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

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

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)

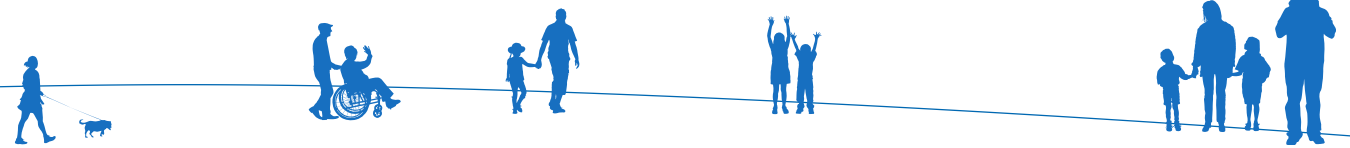
Reference Material (RS)

Impurities (IM)

Drug Product (DP)

Facilities

Analytical Procedures



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Standard subsections

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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/shelf-life

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

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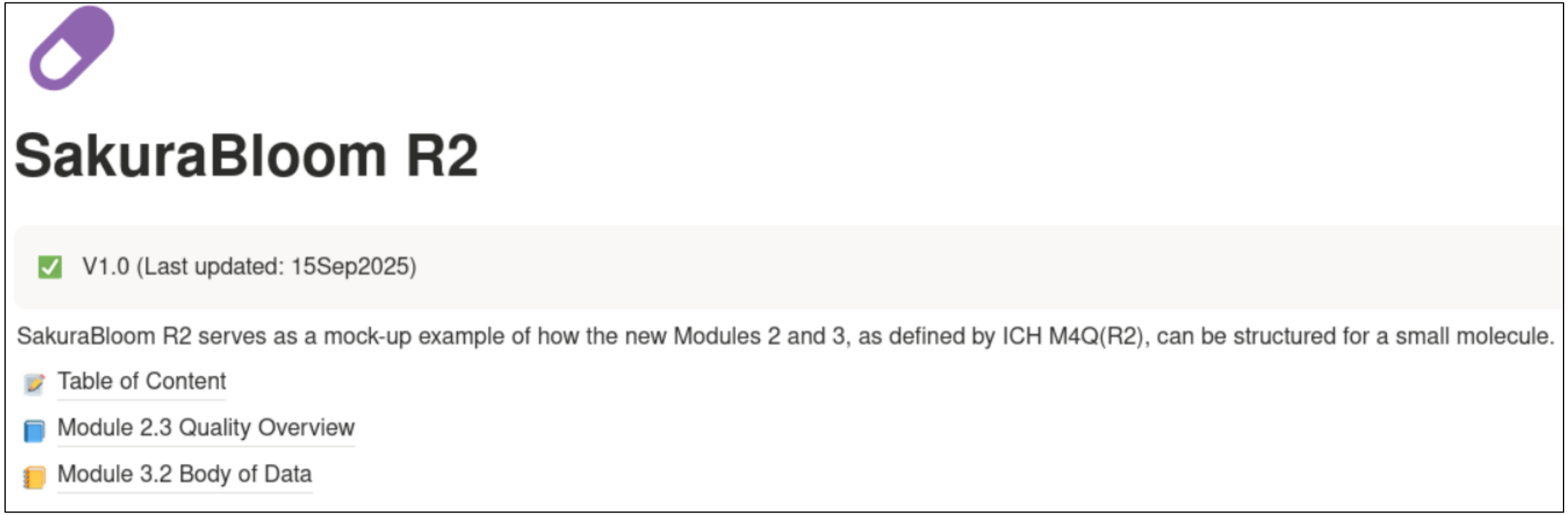
https://www.ich.org/page/ctd

Mock-up

https://ich.org/page/ich-m4qr2-mock-ups



SakuraBloom R2

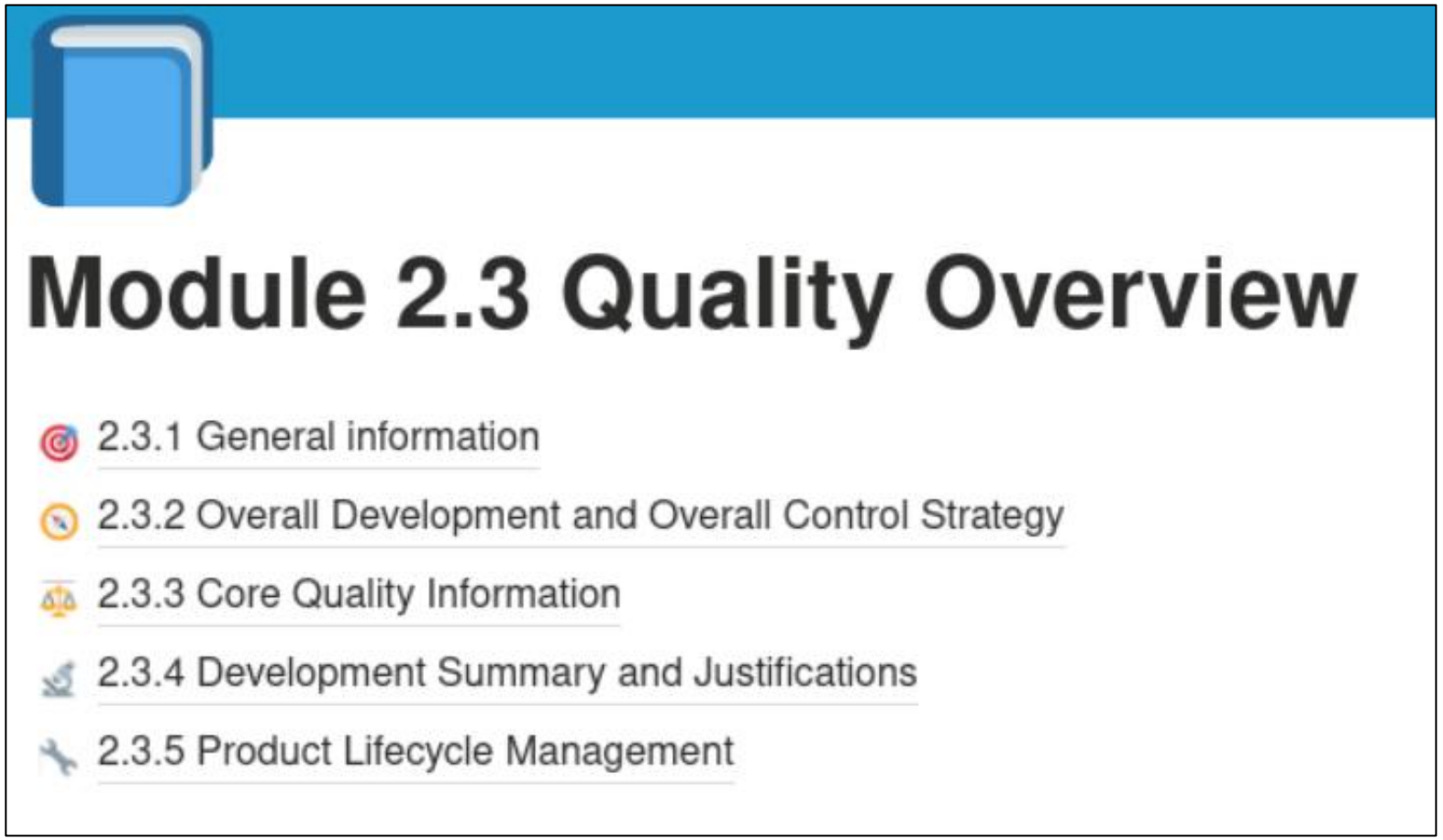
✅ V1.0 (Last updated: 15Sep2025)

SakuraBloom R2 serves as a mock-up example of how the new Modules 2 and 3, as defined by ICH M4Q(R2), can be structured for a small molecule.

- Table of Content
- Module 2.3 Quality Overview
- Module 3.2 Body of Data

Mock-up

https://ich.org/page/ich-m4qr2-mock-ups



Mock-up

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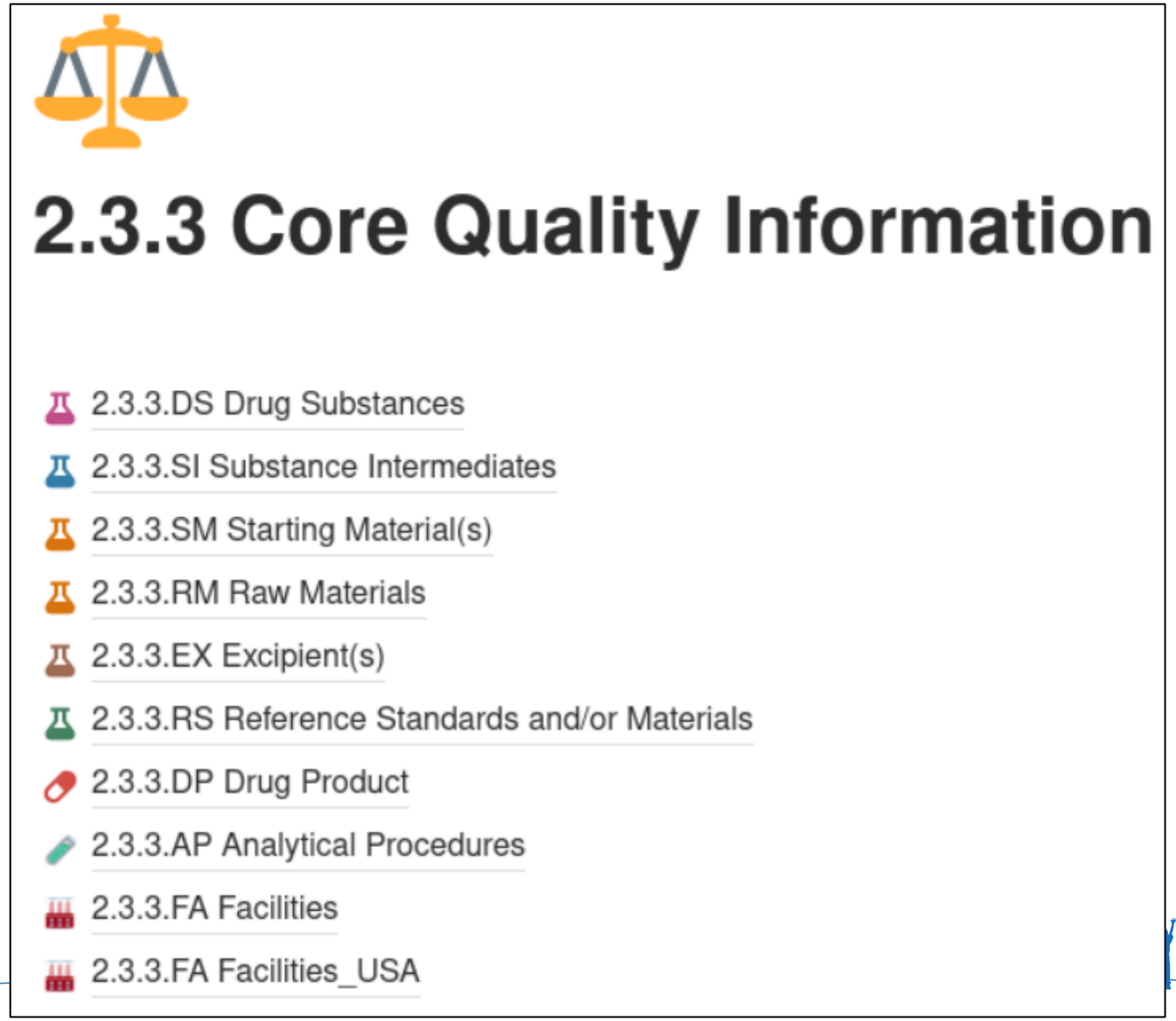

Summary

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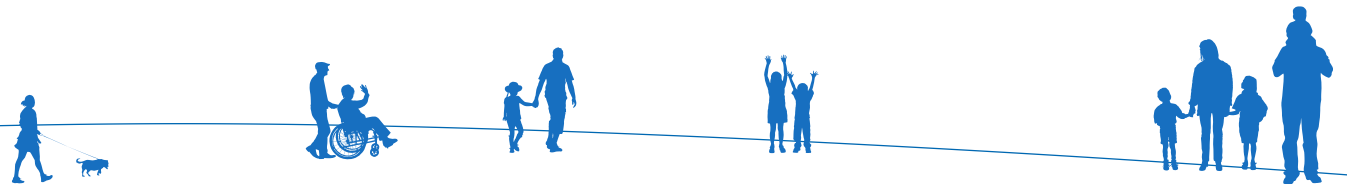
- ICH Q12 was implemented in Japan.
  Usage of ICH Q12 elements is expected to make lifecycle management more efficient.

△ One of the objectives of ICH Q12

- Public consultation of ICH M4Q (R2) has been done by the end of Nov.
  ICH M4Q (R2) aims to enhance lifecycle management and knowledge management.

▽

Based on ICH Q12 and M4Q (R2), we need to discuss how we achieve more efficient lifecycle management.



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