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ICH Q12 (Pharmaceutical Product Lifecycle Management): PMDA Perspective

Yasuhiro Kishioka, Ph.D.

Principal Reviewer

Office of Cellular and Tissue-based Products

PMDA

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ICH Quality Vision 2003

Develop a harmonised pharmaceutical quality system applicable across the life cycle of the product emphasizing an integrated approach to quality risk management and science

➔ ICH Q8~Q11, Points to Consider, Q&As

[Current Situation]

- ▶ The envisioned post-approval 'operational flexibility' has not been achieved as the main emphasis at ICH to date has focused on early stages of the product lifecycle.
- ▶ The lack of harmonised approaches for technical and regulatory aspects for lifecycle management can hinder innovation and continual improvement.

➔ ICH Q12: Pharmaceutical Product Lifecycle Management

Objectives and Scope



► Objectives include:

- Provide a framework to facilitate the management of post-approval Chemistry, Manufacturing and Controls (CMC) changes in a more predictable and efficient manner across the product lifecycle
- Optimization of industry and regulatory resources
- Support innovation and continual improvement and help to assure drug product supply

► Scope

Pharmaceutical products, including currently marketed chemical, biotechnological and biological products. (However, each regulatory authority will decide whether generic medicines can be included in the scope of this guideline.)

Issues to be addressed in ICH Q12

From ICH Q12 Concept Paper

► Regulatory Dossier

- Explore the development of a harmonised approach to “regulatory commitments” for inclusion in the guideline. Such approaches could enable post approval changes that facilitate continual improvement and encourage the adoption of innovative technologies.
- Delineate the appropriate level of detail and information necessary for regulatory assessment and inspection in the dossier, in order to create a more enabling post approval change management system.

► Pharmaceutical Quality System (PQS) aspect

- Establish criteria for a harmonised risk-based change management system based on product, process and/or clinical knowledge that effectively evaluates the impact of change on quality, and, as applicable to safety and efficacy.
- Clarify expectations and reinforce the need to maintain a knowledge management system that ensures continuity of product and process information over the product lifecycle.

► Post-Approval Change Management Plans and Protocols

- Introduce the concept of a post-approval management plan that can be used to proactively identify post-approval changes and the mechanism to submit and assess these changes by regulatory authorities (Assessors and Inspectors)
- Establish criteria for post-approval change management protocols that can be adopted by the ICH regions (enabling a harmonised proactive approach for lifecycle management)
- Encourage enhanced product development and control strategy approaches (Quality by Design (QbD)) providing opportunities for scientific and risk based foundations for post-approval change management plans.

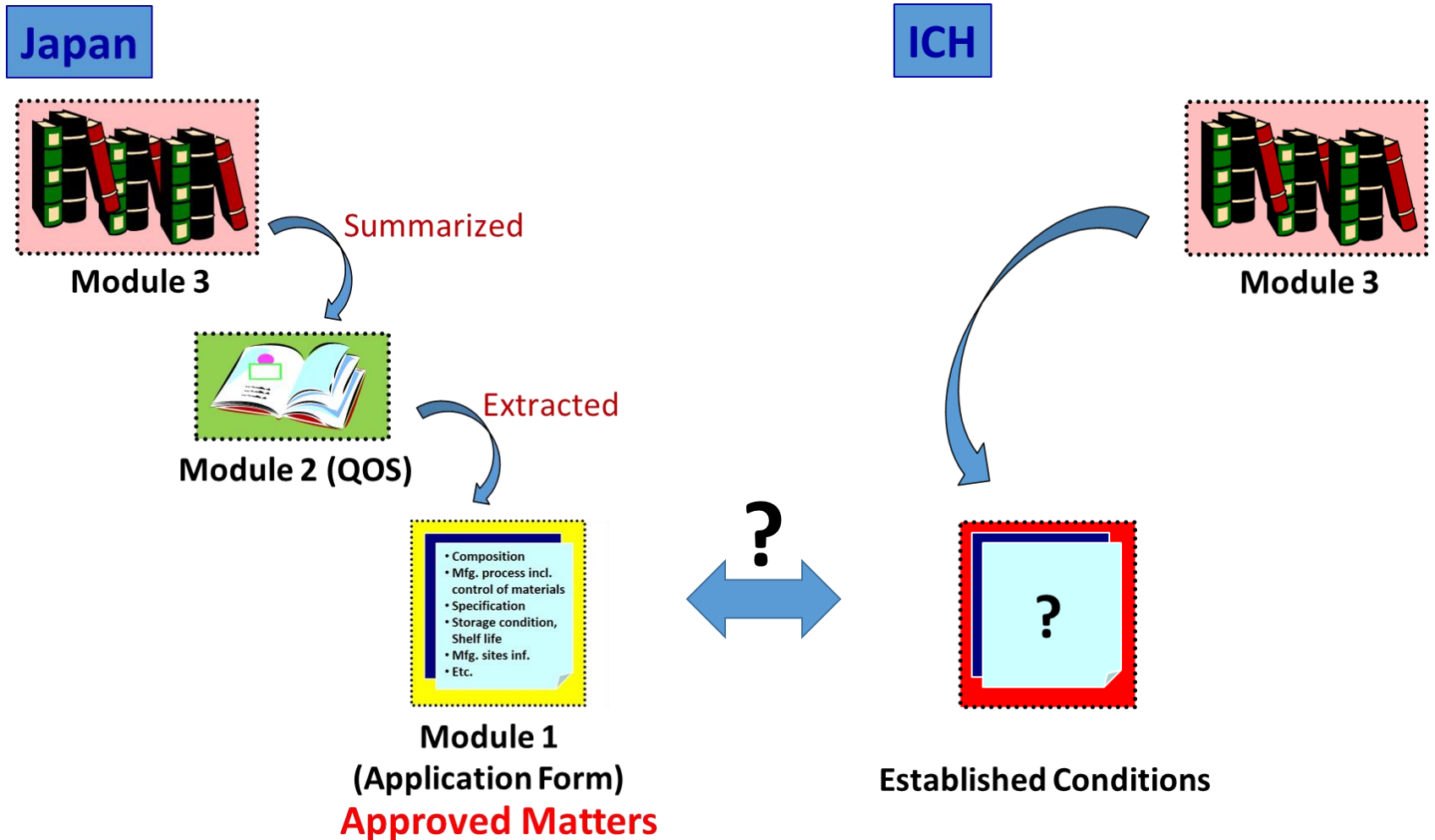
Regulatory Commitments/Established Conditions

▶ Although the Common Technical Document (CTD) format has been defined for a marketing application, there are no previously harmonised approaches to defining what changes would require a regulatory submission.

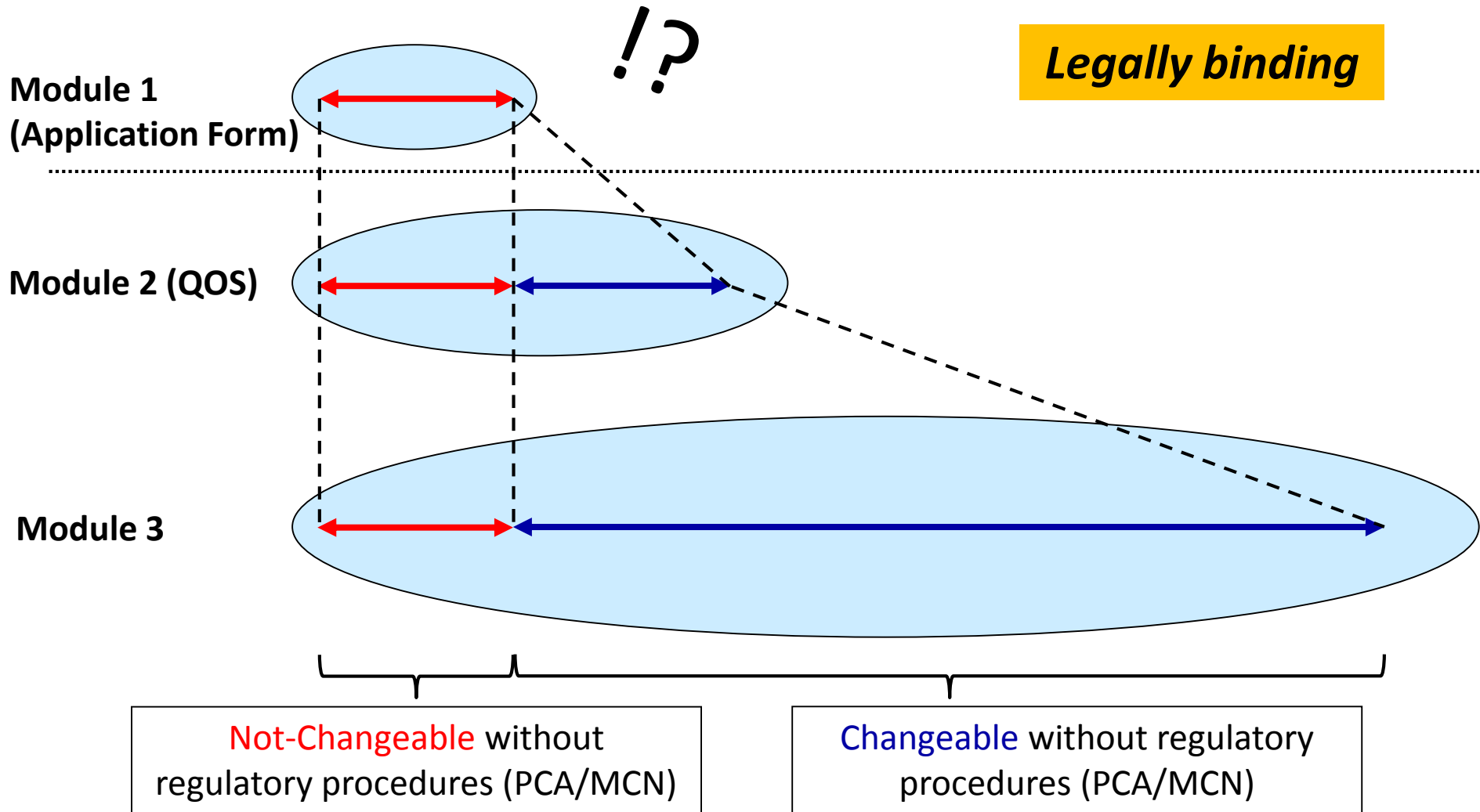
▶ Established Conditions

- are legally binding information (or approved matters) considered necessary to assure product quality.
- are contained in a regulatory submission, proposed by the applicant, and approved by the regulatory authority.
- As a consequence, any change to Established Conditions necessitates a submission to the regulatory authority that is consistent with regional regulations or guidance; or as agreed upon during review and approval of the marketing application.

Approved Matters and Established Conditions

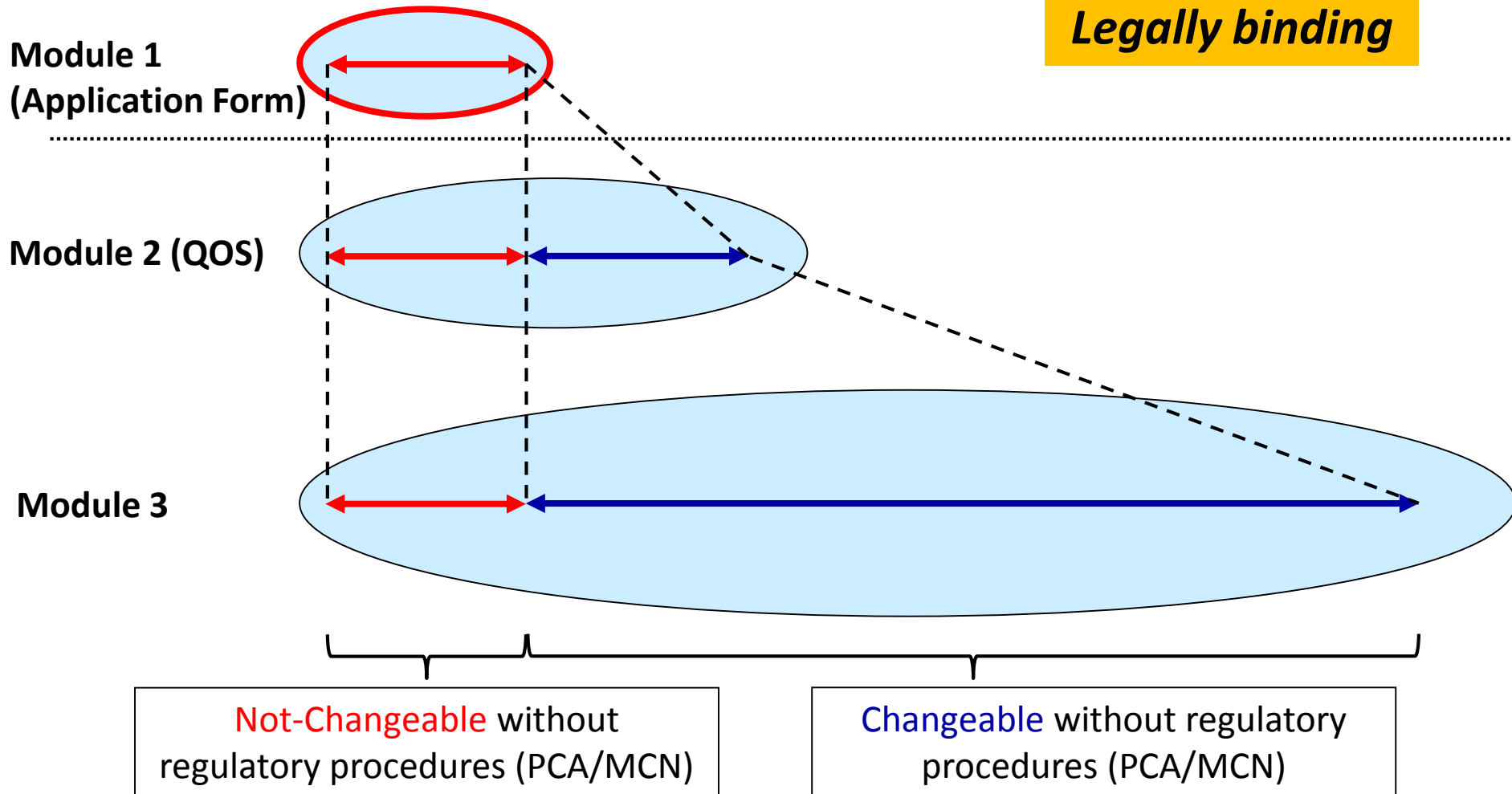


Japan's Effective/Efficient/Flexible Quality Regulation



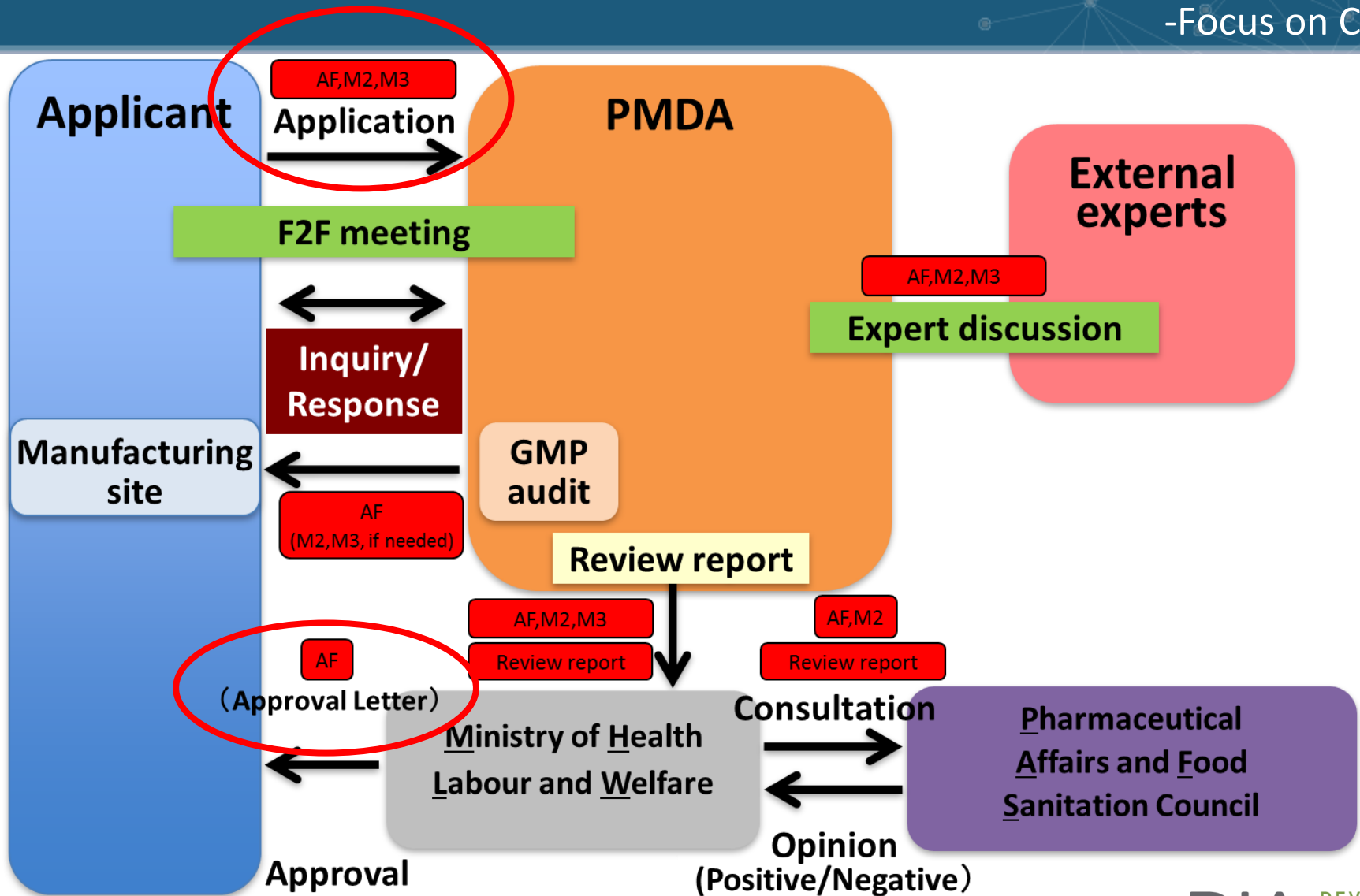
Japan's Effective/Efficient/Flexible Quality Regulation

Legally binding



Review Process of MAA with document flow

-Focus on CMC-

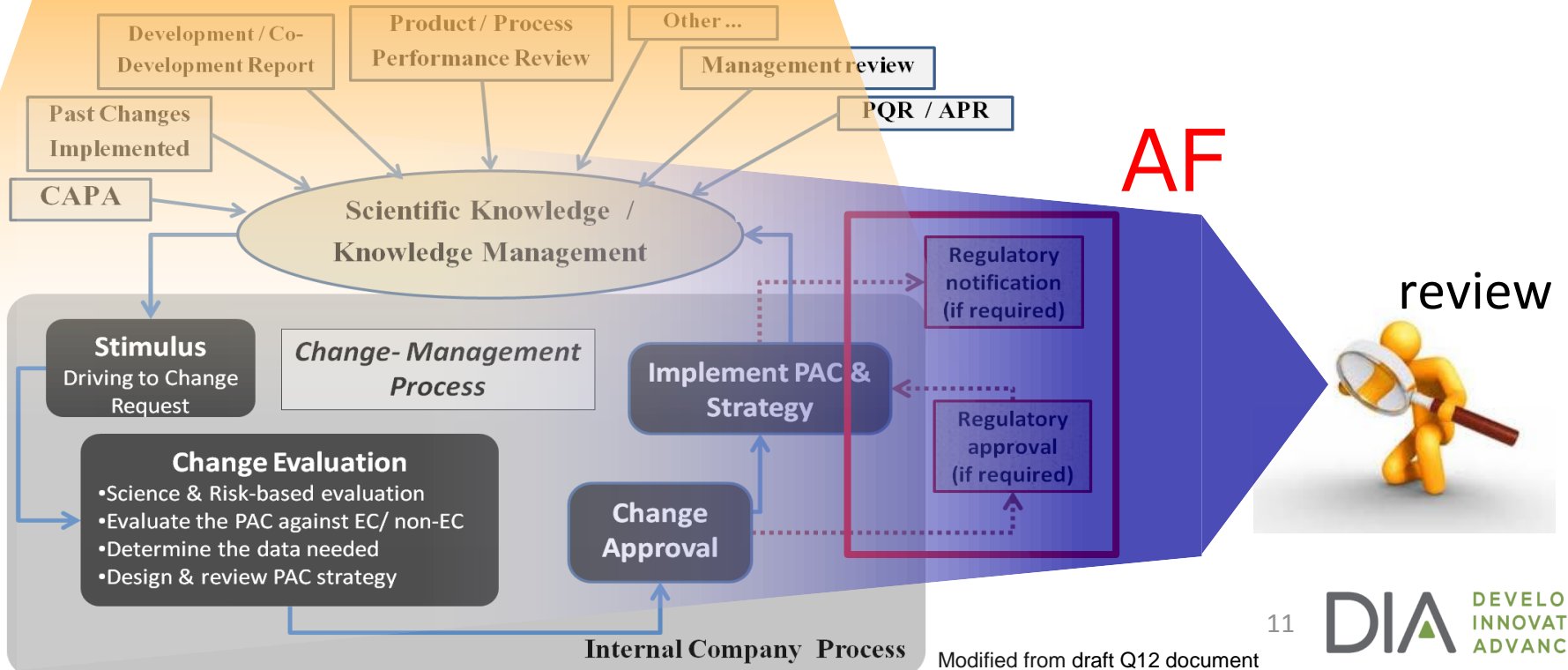


AF and Review/Inspection

-Focus on post-approval change-



inspection



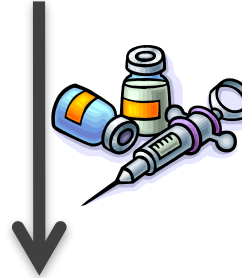
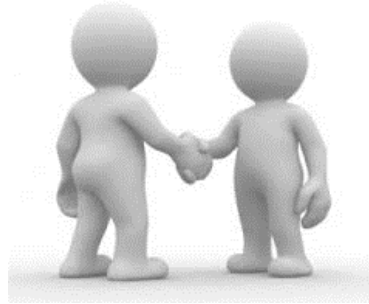
Japanese Application Form

MHLW



- Composition
- Mfg. process incl. control of materials
- Specification
- Storage condition, Shelf life
- Mfg. sites inf.
- Etc.

MAHs



Japanese Application Form/Approved Matters

- ▶ Application Form (AF), found in Module 1.2, is a legally binding document in Japan.
- ▶ Essential elements to ensure pharmaceutical quality should be described in AF.
- ▶ A post-approval regulatory action is required if a MAH changes the content in the AF (Approved Matters; AMs).
- ▶ AMs (incl. PCA/MCN) are determined on a product-by-product basis.
- ▶ AF provides the transparency and flexibility in terms of post-approval changes.

Product Specific Lifecycle Management Strategy

▶ The document summarizes the information relating to the lifecycle management strategy for the product in one location.

- Established Conditions (ECs)
- Report category for making changes of approved ECs
- Post-Approval Change management Protocols
- Post-approval CMC commitments (if applicable)

At the MAH's discretion, the PSLCMS may also proactively identify some of the company's anticipated post approval changes.

▶ It allows both MAHs and Regulatory Authorities to plan well in advance of implementing post-approval changes relevant to a product's ECs.

Product Specific Lifecycle Management Strategy

	Current
Established Conditions	M1.2
Post-approval change (PAC) reporting categories	M1.2
Post-Approval Change Management Protocols (PACMPs)	N/A
Post-approval CMC commitments, if applicable	Response to inquiry, Memorandum
Anticipated PAC	N/A

Product Specific Lifecycle Management Strategy

Japan



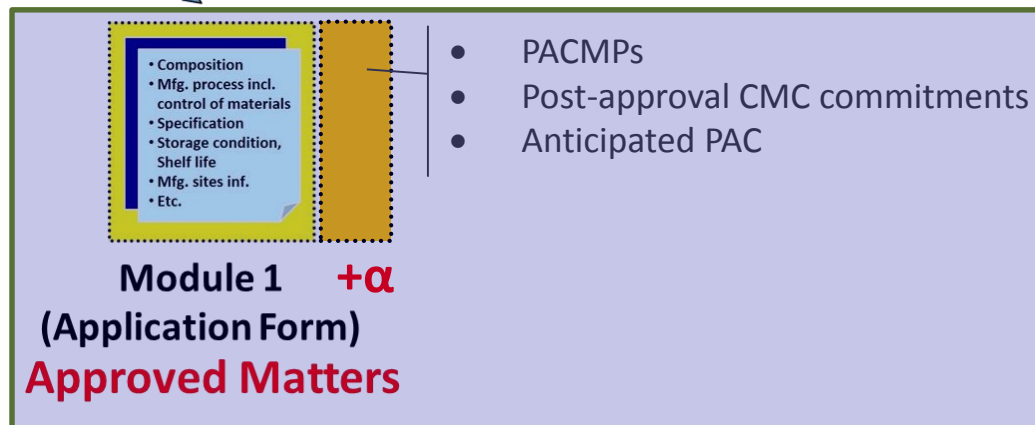
Module 3

Summarized



Module 2 (QOS)

Extracted

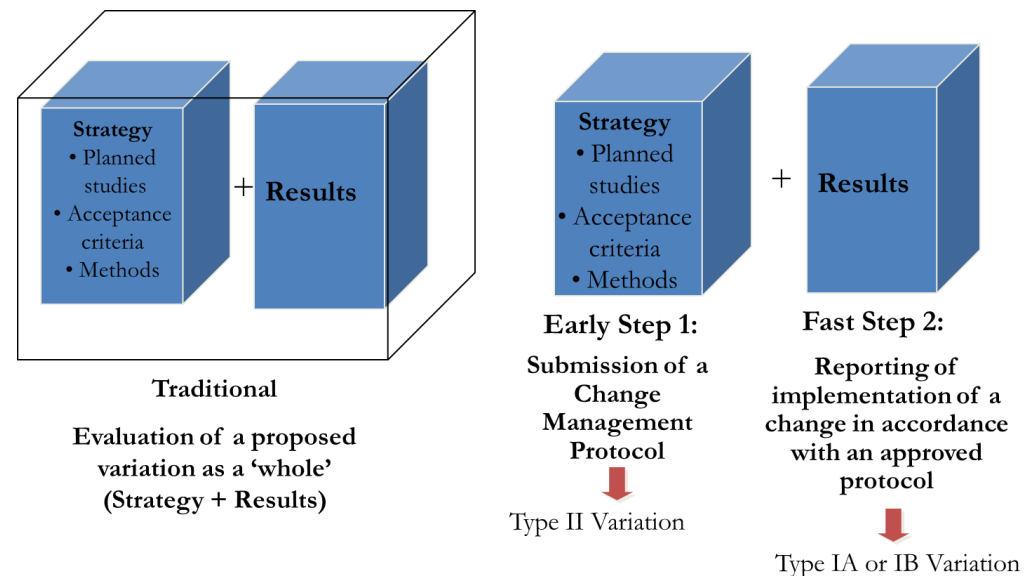


Product Specific Lifecycle Management Strategy???

Post Approval Change Management Protocol

- ▶ a regulatory tool that provides predictability and transparency in terms of the requirements and studies needed to implement a change.

Questions and answers on post approval change management protocols
(EMA/CHMP/CVMP/QWP/586330/2010)



- ▶ PMDA has been considering the adoption of PACMP.

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Ask

