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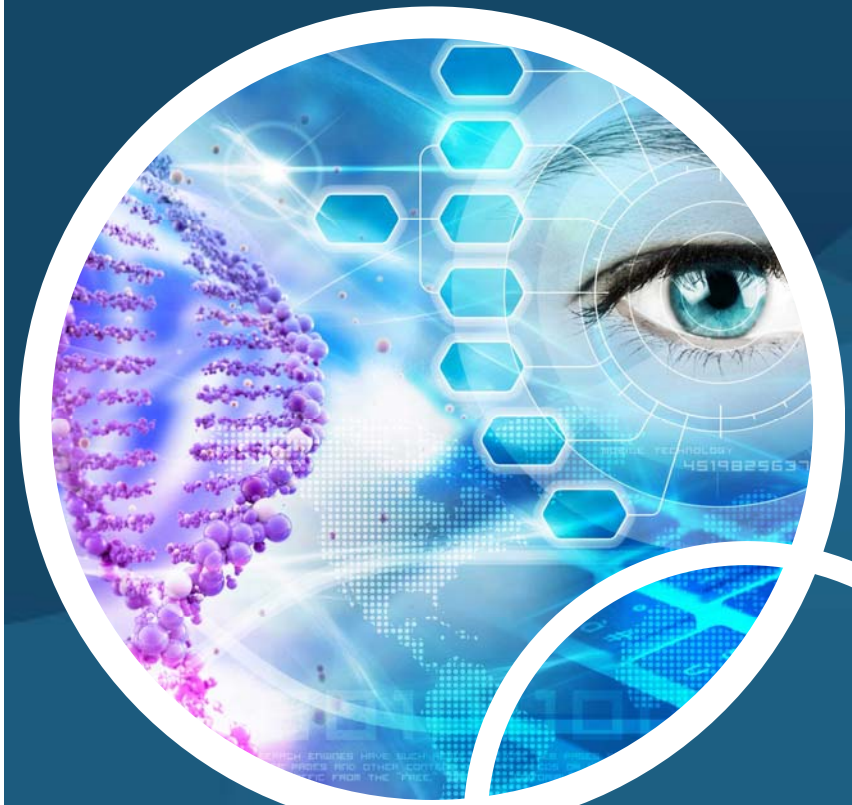

ICH Q12 (Pharmaceutical Product Lifecycle Management): PMDA Perspective

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Background

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

[Potential Opportunity] (ICH Q10 Annex 1)

- optimise science and risk based post-approval change processes to maximise benefits from innovation and continual improvement.

[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 harmonized approaches for technical and regulatory aspects for lifecycle management can hinder innovation and continual improvement.

➡ ICH Q12: Pharmaceutical Product Lifecycle Management

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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.

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ICH Q12 activity so far

- 2014 November – to date
  - Six (6) ICH F2F meetings
  - Two (2) Interim meetings
- 2017 June: Step1 (Agreement among EWG members)

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Step 1 document - Core Guideline (35 pages)-

1. Introduction
2. Categorization of Post-approval CMC Changes
3. Established Conditions (ECs)
4. Post-Approval Change Management Protocol (PACMP)
5. Product Lifecycle Management (PLCM)
6. Pharmaceutical Quality System and Change Management
7. Relationship between Regulatory Assessment and Inspection
8. Post-approval Changes for Marketed Products
9. Glossary
10. References

Appendix1: CTD Sections that contain ECs

Appendix2: Principles of Change Management

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Step 1 document - Annex (19 pages)-

Annex I: ECs- Illustrative Examples
- Annex IA: Chemical Product
- Annex IB: Biological Product

Annex II: PACMP- Illustrative Examples
- Annex IIA: PACMP Example 1
- Annex IIB: PACMP Example 2

Annex III: PLCM Document- Illustrative Examples

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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 drug substances (i.e., active pharmaceutical ingredients) and pharmaceutical drug products, including marketed chemical, and biotechnological/biological products.
  - The guideline also applies to drug-device combination products that meet the definition of a pharmaceutical or biotechnological/biological product.
  - Changes needed to comply with revisions to pharmacopoeial monographs are not in scope of this guideline.

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ICH Q12 Regulatory Tools and Enablers

- Provide a framework to facilitate the management of post-approval CMC changes in a more predictable and efficient manner across the product lifecycle
- Regulatory Tools and Enablers
  - Categorization of Post-approval CMC Changes
  - Established Conditions (ECs)
  - Post-Approval Change Management Protocol (PACMP)
  - Product Lifecycle Management (PLCM)
  - Pharmaceutical Quality System and Change Management
  - Relationship between Regulatory Assessment and Inspection
  - Post-approval Changes for Marketed Products

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Established Conditions (ECs)

- Although the Common Technical Document (CTD) format has been defined for a marketing application, there are no previously harmonized approaches to defining which elements in an application are considered necessary to assure product quality and therefore would require a regulatory submission if changed post-approval.
- These elements are being defined in this guideline as “Established Conditions for Manufacturing and Control” (referred to as ECs throughout this guideline).
- ECs are legally binding information (or approved matters) considered necessary to assure product quality. As a consequence, any change to ECs necessitates a submission to the regulatory authority.

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Established Conditions (ECs)

- CTD sections that contain ECs (Appendix 1)
- Identification of ECs for the Mfg. Processes (Section 3.2.3.1, Annex I)
- Identification of ECs for Analytical Procedures (Section 3.2.3.2)
- Revisions of ECs (Section 3.2.4)
- Roles and Responsibility (Section 3.3)
  - The management of all changes to and maintenance of the approved marketing application is the responsibility of the MAH.
  - There is a joint responsibility to share and utilize information b/w the MAH and any manufacturing organizations to assure the marketing application is maintained, reflects current operations, and that changes are implemented appropriately across relevant sites.
  - Maintenance of the marketing application (including aspects that are not identified as ECs) should follow regional expectations.

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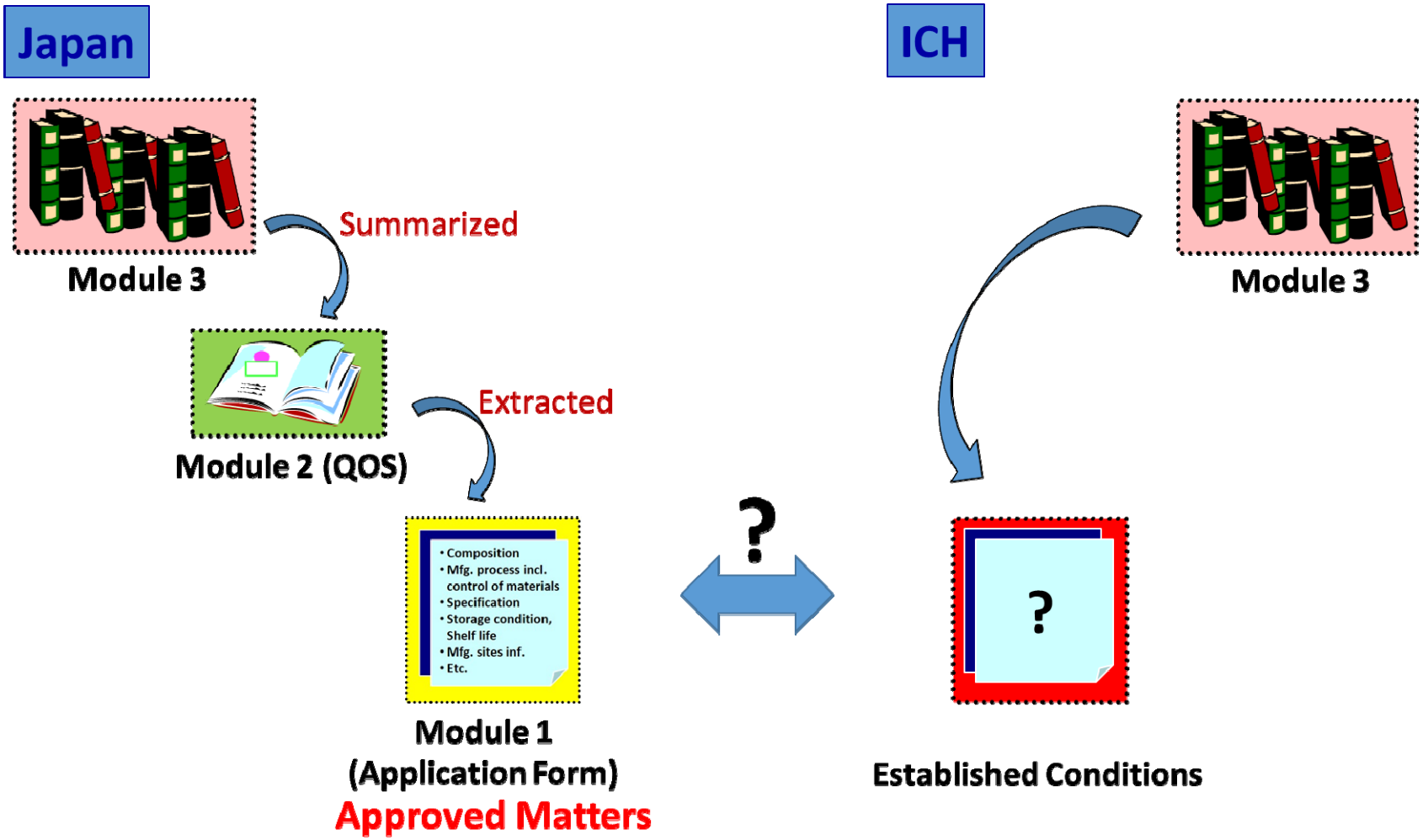
Approved Matters and Established Conditions



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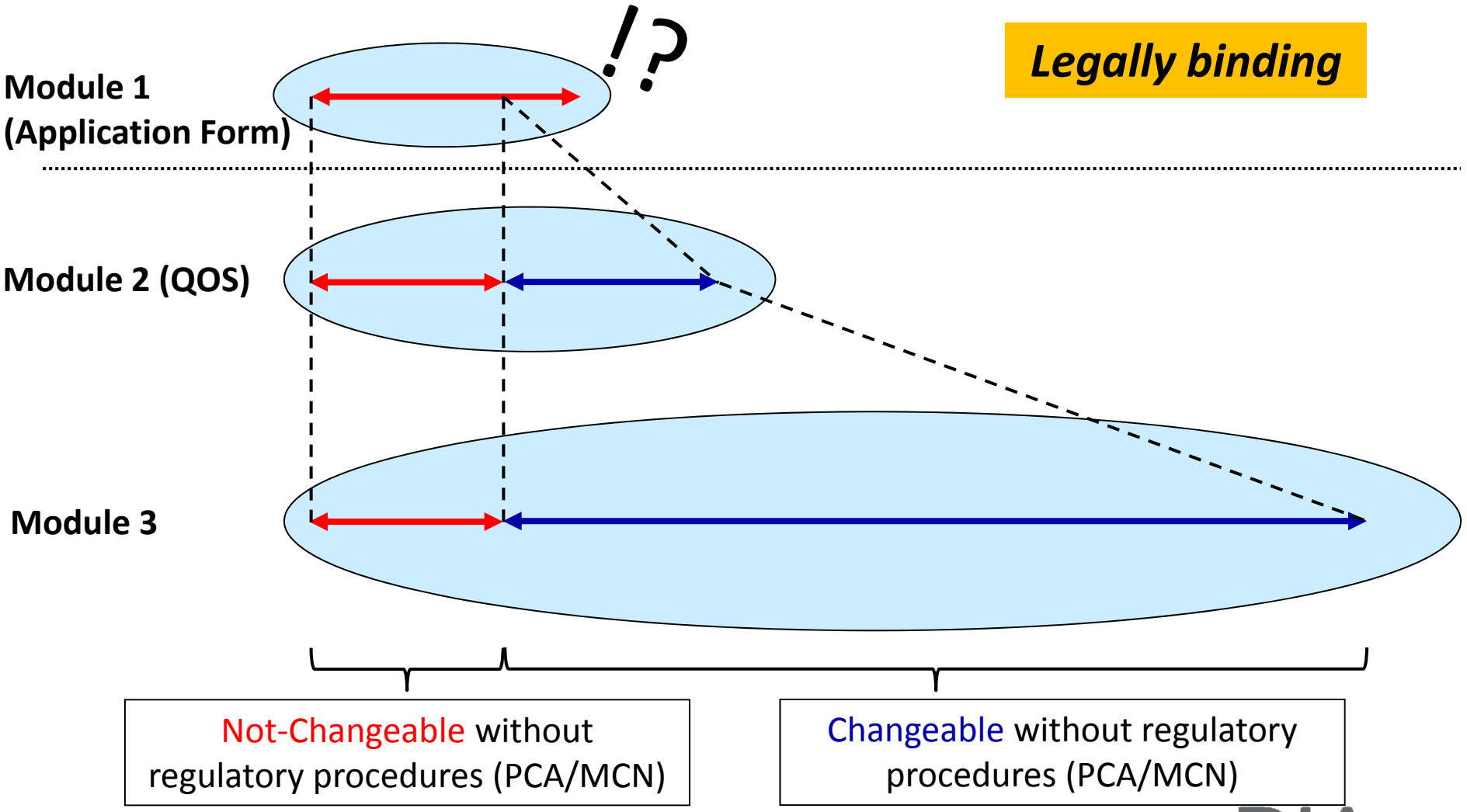
Rational Regulatory Oversight in Japan



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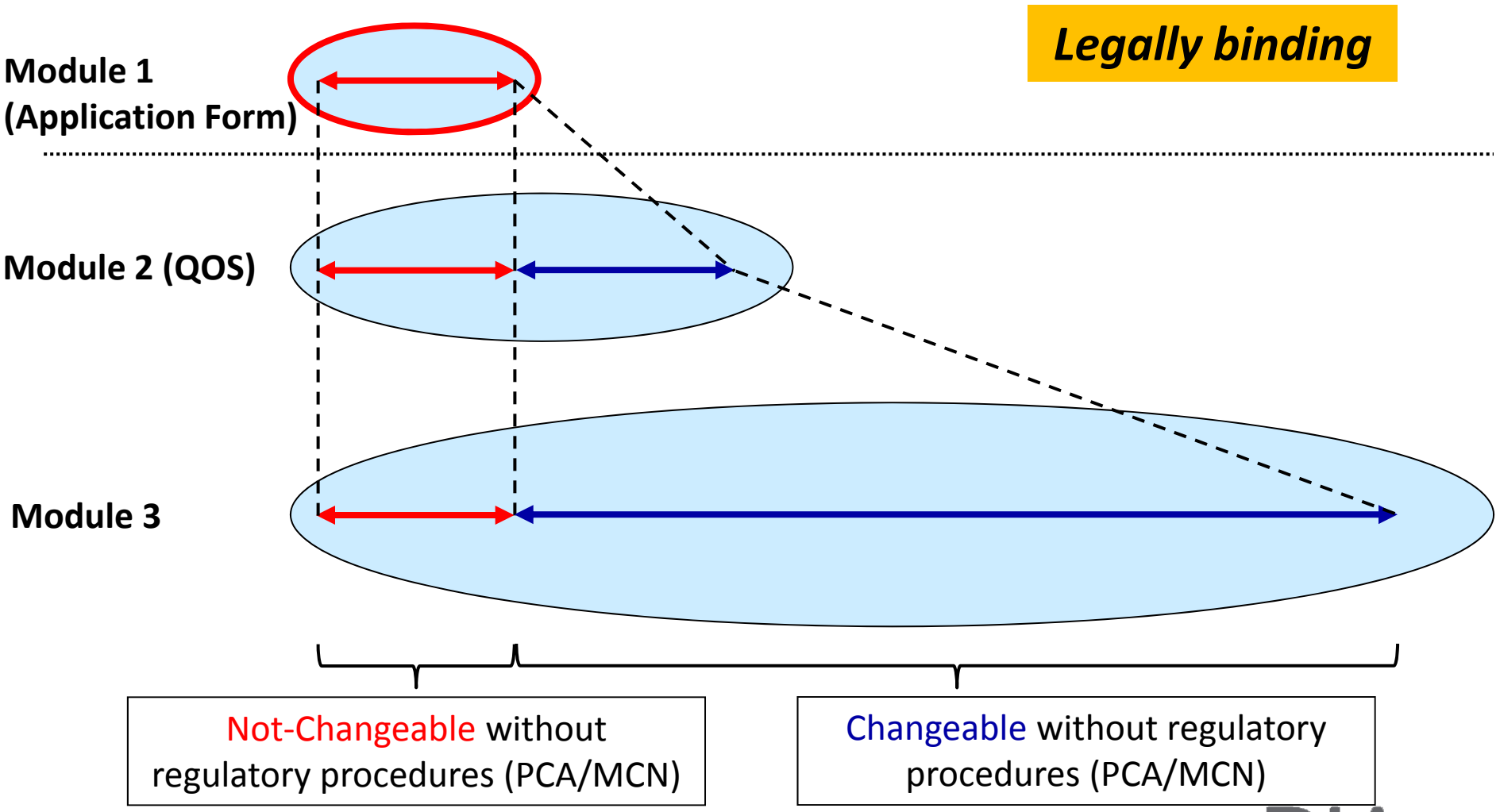
Rational Regulatory Oversight in Japan



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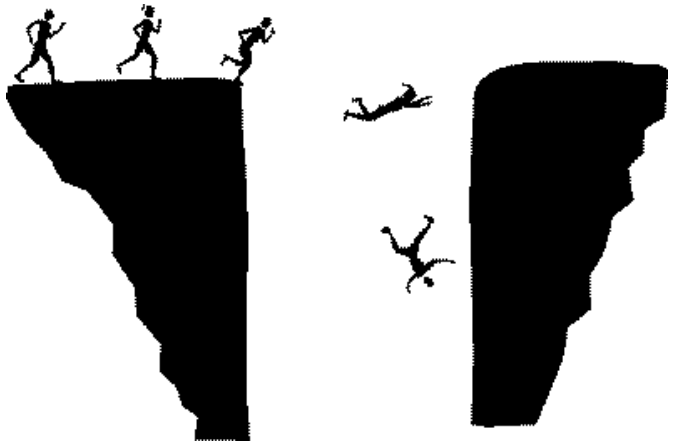
My Expectations...

Current



Development Post-Approval

Future

Development Post-Approval

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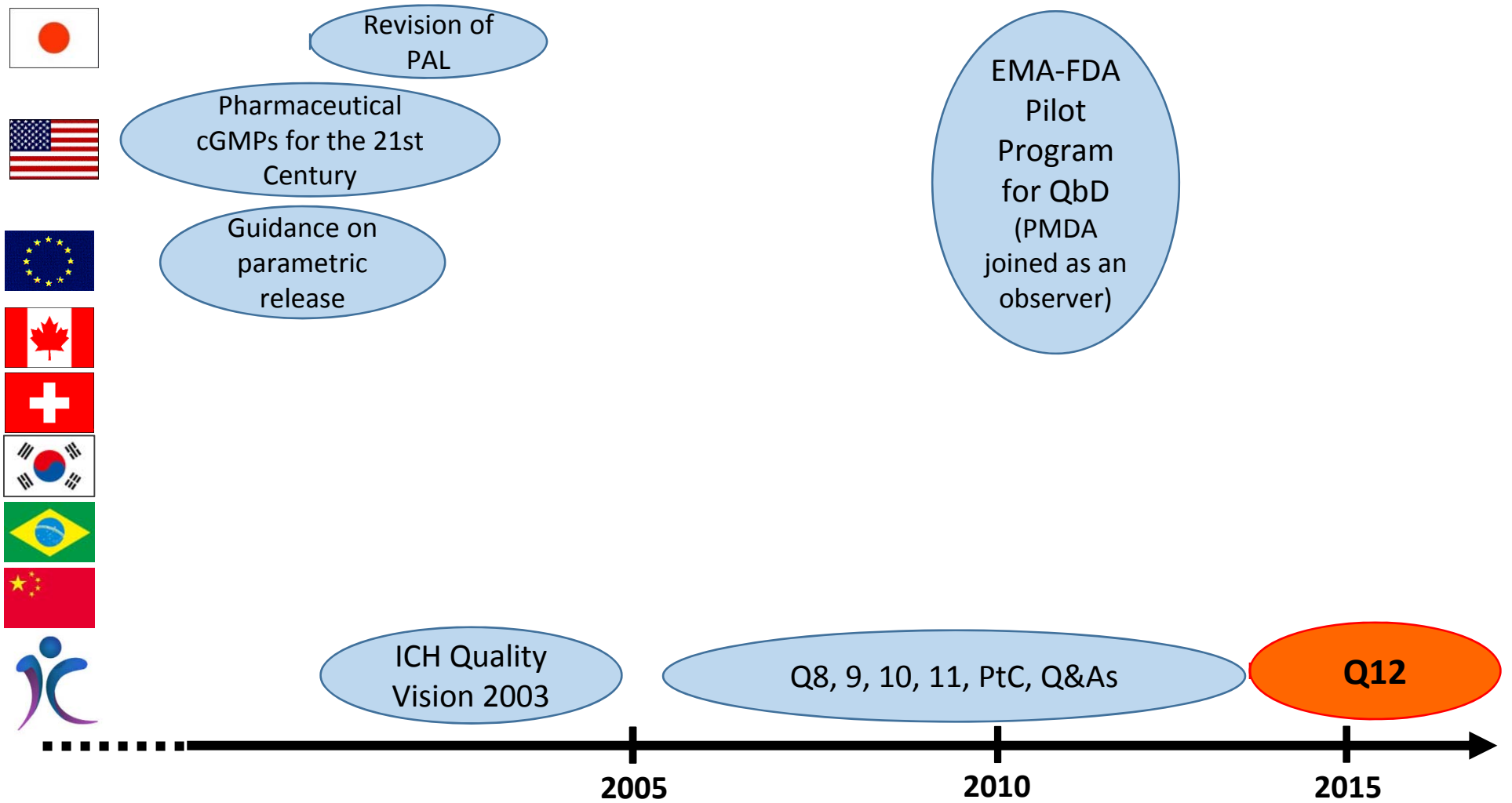
Regional initiatives and ICH activities



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Ask