PMDA Updates

- with a focus on GMP/CMC -

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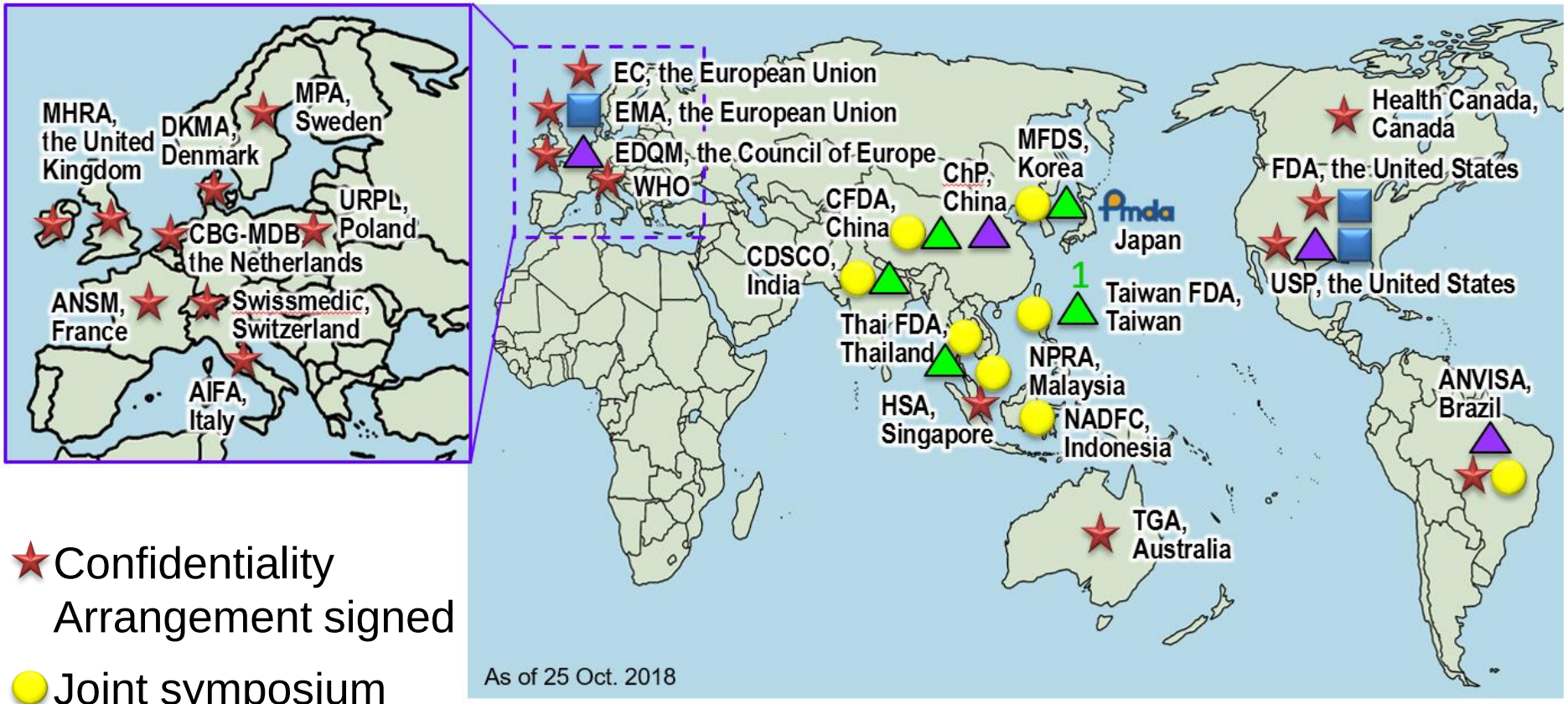
The views and opinions expressed in this presentation are those of the presenter and should not necessarily represent the views and opinions of the PMDA.

Outline

- PMDA's International Activities
- Toward ICH Q12 Implementation

PMDA's Bilateral Cooperation



★ Confidentiality Arrangement signed

● Joint symposium held

■ PMDA staff stationed at the agency

▲ Cooperative Arrangement on cooperation of pharmacopoeia signed

▲ Cooperative Arrangement signed

Japan-EC*1 Mutual Recognition Agreement (MRA)

*1:In accordance with the Exchange of Notes Verbales between Japan and the EU in 2010, the word "European Community" in the Agreement was replaced with "European Union."

- This is the first bilateral agreement on mutual recognition for Japan, covering 4 sectors (i.e. telecommunications equipment, electrical products, Good Laboratory Practice (GLP) for chemicals and Good Manufacturing Practice (GMP) for Medicinal Products)
- **January 1, 2002** – The agreement came into force.
- **May 29, 2004** – Provisions on GMP for Medicinal Products became operational upon the completion of Sectoral Annex on GDP. Applicable scope was Chemical Pharmaceuticals (excluding active pharmaceutical ingredients and sterile medicinal products).
- **April 2016** - MRA countries expanded from 15 to 28 (all EU member states)
- **July 2018** - Operational scope extended from only Chemical Pharmaceuticals to Sterile Medicinal Products, Active Pharmaceutical Ingredients and Biological Pharmaceuticals*2.

*2:Except following pharmaceuticals
1. pharmaceuticals derived from human blood, tissue and cells from unspecified donor
2. pharmaceuticals derived from transgenic animals and plants

PMDA's Multilateral Cooperation

APEC

APAC RHSC

IMDRF

PIC/S

pmda

IPRP
International Pharmaceutical Regulators Programme

OECD/GLP
BETTER POLICIES FOR BETTER LIVES

ICMRA
International Coalition of Medicines Regulatory Authorities

ICH
harmonisation for better health

2019 PIC/S Committee Meeting and Seminar to be held in Toyama city, Japan

PIC/S Committee Meeting

Date: 11-12 November 2019

PIC/S Seminar 2019

Date: 13-15 November 2019

Theme: “Quality Assurance of Sterile Medicinal Products -Annex1-”

Objectives:

1. To explain and discuss content of revised Annex 1 and issues which were raised during revision.
2. Through the case study of sterility assurance, to learn how to consider risk based validity.
3. To introduce advanced technologies for sterility assurance and the way of control

ICH: Ongoing Activities

- ICH produced over 60 Guidelines on technical requirements.
- Over 20 WGs are now ongoing.

Safety	Quality	Efficacy	Multidisciplinary
S1(R1)	Q3C(R8)	Standing Paediatric	M1
S5(R3)	Q3D(R1)/(R2)	E2B(R3)	M2
S11	Q11	E8(R1)	M4Q(R1)
	Q12	E9(R1)	M7(R2)
	Q13	E11A	M8
	Q2(R2)/Q14	E14	M9
		E19	M10
		E20	M11
			M12

ICH Q12 Regulatory Tools & Enablers

Provide a framework to facilitate the management of post-approval CMC changes in a more predictable and efficient manner across the product lifecycle

- Categorization of Post-approval CMC Changes
- Established Conditions (ECs)
- Post-Approval Change Management Protocol (PACMP)
- Product Lifecycle Management (PLCM)
- Pharmaceutical Quality System (PQS) and Change Management (CM)
- Relationship between Regulatory Assessment and Inspection
- Post-approval Changes for Marketed Products

How We Address These Challenges?

November 2014

ICH Q12

May 2015

PMDA ICH Q12 WG

December 2014

AMED

AMED Research Group

September 2016

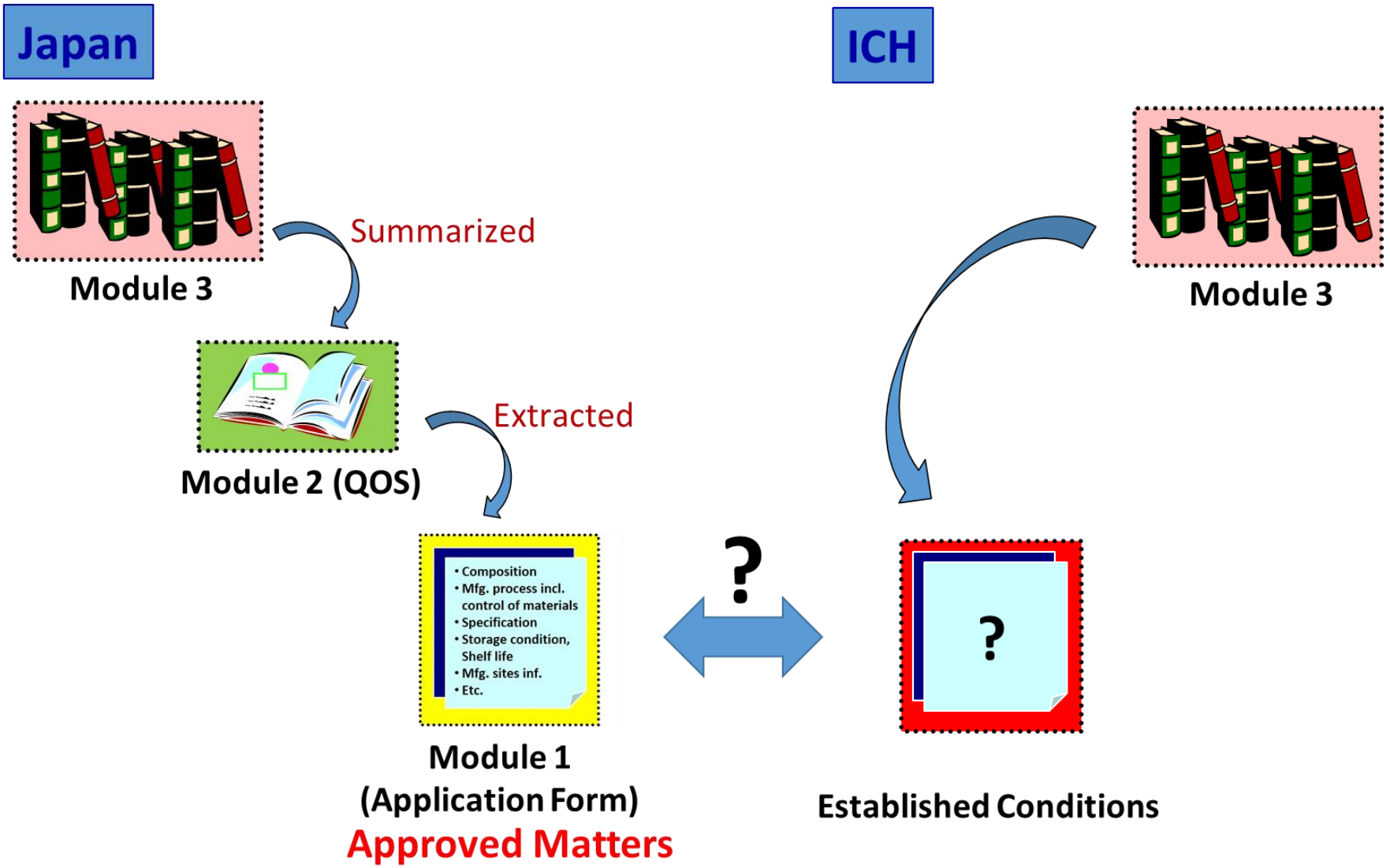
MHLW/PMDA-FPMAJ Task Force

AMED: Japan Agency for Medical Research and Development
MHLW: Minister of Health Labour and Welfare
FPMAJ: The Federation of Pharmaceutical Manufacturers' Associations of JAPAN

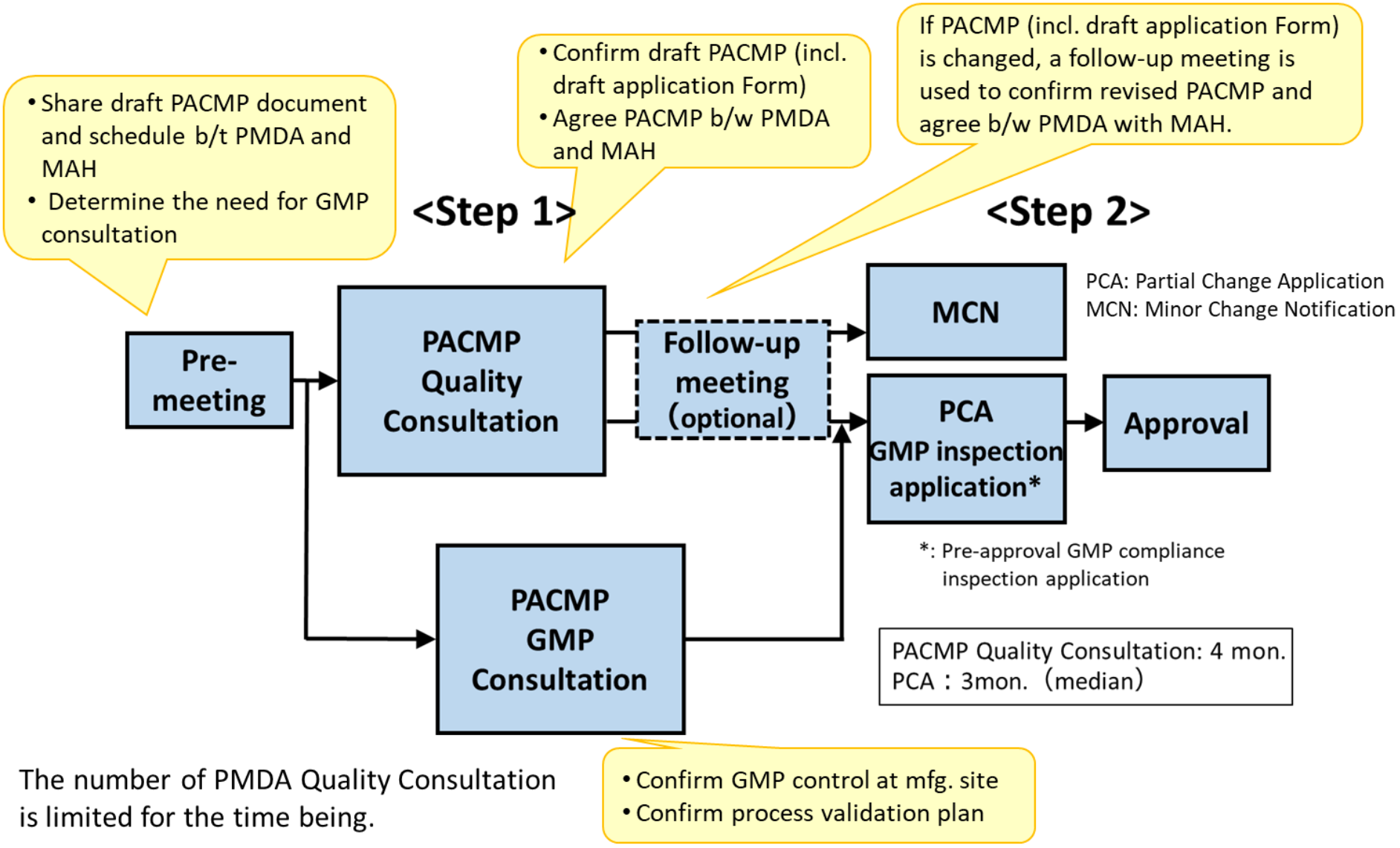
Overview of Three Main Activities

- PMDA ICH Q12 WG (established in May 2015)
  - Members: Reviewers (chemical, biologic, generic), Inspectors
  - Discuss regulatory, technical and practical issues within PMDA
- AMED Research Group (joined since December 2014)
  - Members: Academia, Industry, PMDA
  - Discuss technical and practical issues
  - Report the outcome and proposal to MHLW
- MHLW/PMDA-FPMAJ Task Force (established in September 2016)
  - Members: MHLW, PMDA, FPMAJ
  - Driven by *"domestic problems"* (not by ICH Q12)
  - Streamline the regulatory procedures for post-approval CMC changes

Approved Matters and Established Conditions



Overview of PACMP pilot program in Japan



The number of PMDA Quality Consultation is limited for the time being.

Review of PMD Act

Theme 1: Ensuring early access to innovative pharmaceuticals & medical devices, and enhancing the safety measures

(1) Streamline of Approval Process for early patient access

① "Conditional Early Approval System" and "SAKIGAKE Review Designation" should be legislated to clarify process and raise transparency.

② New Approval system for Medical Devices to reflect the characteristics of medical devices (considering innovative technologies; Big Data, AI etc.,)

③ Clarification of Clinical Trials Process

(2) Introduction of new Quality Management System

① Introduction of GMP and GCTP inspection per manufactory

② Revision of current QMS inspection

③ **Introduction of Change Management Method for Quality of approved products using PACMP**

(3) Strengthen Safety Measures

① Provide electronic information of Package Inserts

② Increase traceability of pharmaceuticals and medical devices

③ Utilize Patient Registry Data For safety measure

Product Lifecycle Management (PLCM) document

- a summary that transparently conveys to the regulatory authority how the MAH plans to manage post-approval CMC changes.

- Elements of PLCM document
  - Summary of Product Control Strategy
  - ECs
  - Reporting Categories for making changes to approved ECs
  - PACMPs
  - Post-approval CMC Commitments

(Current perspective) PLCM document in Japan

Japan

Module 3

Summarized

Module 2 (QOS)

Extracted

Product Lifecycle Management document??

Module 1 (Application Form) **Approved Matters**

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- Summary of Product Control Strategy
- PACMPs
- Post-approval CMC commitments

Asia Training Center for Pharmaceuticals and Medical Devices Regulatory Affairs

- Plan, design and coordinate training for Regulatory Authority staffs (established in 2016)
- Provide **training opportunities** including **on-site training**

⇨
- Help raise the level of Regulations in Asia and the world.
- **In FY2017, 235 regulators from 27 countries/regions participated.**

(50% increase from 2016)

Training seminar seminars to Regulatory Authority members by PMDA

PMDA Office

Outside Japan

APEC regions

Lectures, case studies, and on-site training

Establishing a centralised training center for multi-regional clinical trials

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PMDA Asia Training Center: Training Seminar (April 2018 - March 2019)

	Contents	Date	Location
1	Pediatric Review*	June 11-14, 2018	Tokyo (PMDA)
2	Pharmaceuticals Review	June 18-22, 2018	Tokyo (PMDA) and Toyama Prefecture
3	Good Registration Management (GRM)**	September 26-28, 2018	Taipei
4	Pharmaceuticals Review	October 15-16, 2018	Nay Pyi Taw, Myanmar
5	Quality Control (Herbal Medicine)	October 22-24, 2018	Toyama, Toyama Prefecture
6	Medical Devices Review	November 12-16, 2018	Tokyo (PMDA)
7	**Good Manufacturing Practice (GMP) *** **	**November 26-30, 2018**	**Utsunomiya, Tochigi Prefecture**
8	Multi-Regional Clinical Trial (MRCT)**	January 21-24, 2019	Tokyo (PMDA)
9	Pharmaceuticals Review	January 28-31, 2019	Jakarta, Indonesia
10	Pharmacovigilance**	February 4-7, 2019	Tokyo (PMDA)

*Joint Seminar with U.S.FDA, **APEC-LSIF-RHSC CoE Workshop, *** With the support of PIC/S

Key Enablers

- International Cooperation
- Collaboration with Industries

Thank you for your attention!