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.
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

As of 25 Oct. 2018
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
- OECD/GLP
- ICH
- IPRP
- ICMRA
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.

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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 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

Japan

Module 3

Summarized

Module 2 (QOS)

Extracted

Module 1
(Application Form)

Approved Matters

ICH

Module 3

Established Conditions

- Composition
- Mfg. process incl. control of materials
- Specification
- Storage condition, Shelf life
- Mfg. sites inf.
- Etc.
Overview of PACMP pilot program in Japan

**<Step 1>**
- Share draft PACMP document and schedule b/t PMDA and MAH
- Determine the need for GMP consultation

**PACMP Quality Consultation**

**Follow-up meeting (optional)**
- Confirm draft PACMP (incl. draft application Form)
- Agree PACMP b/w PMDA and MAH

**<Step 2>**
- If PACMP (incl. draft application Form) is changed, a follow-up meeting is used to confirm revised PACMP and agree b/w PMDA with MAH.

**MCN**

**PCA GMP inspection application***
- PCA: Partial Change Application
- MCN: Minor Change Notification
- *: Pre-approval GMP compliance inspection application

**Approval**

**PACMP Quality Consultation: 4 mon.**
- PCA: 3mon. (median)

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

**<Step 1>**
- Confirm GMP control at mfg. site
- Confirm process validation plan
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 +α

(Application Form)

Approved Matters

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

- 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

Lectures, case studies, and on-site training

Establishing a centralised training center for multi-regional clinical trials

Outside Japan

APEC regions

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

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<td>June 18-22, 2018</td>
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*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!