International Cooperation and Reliance from Japan's viewpoint

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PMDA

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International Collaboration and Reliance

Significantly important than ever before

- ✓ Globalization of supply chain
- ✓ Emergence of new technologies
- ✓ Limited human resources
- ✓ Response and Preparedness for pandemic (COVID-19 and the Next), etc...

Fast and Stable access to Innovative medical products

International Collaboration and Reliance in Pharmaceutical Regulations

To ensure fast and stable access to products which are effective, safe, quality-assured

- ICH (International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human use)
- ICMRA (International Coalition of Medicines Regulatory Authorities)
- PIC/S (Pharmaceutical Inspection Convention and Pharmaceutical Inspection Co-operation Scheme)
- PDG (Pharmacopoeia Discussion Group)

ICH (The International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human use)

ICH has developed more than 70 guidelines

Recent notable activities

- **GCP renovation (E6(R3))** *step 1*
- **Post-Approval Change Management Protocol [PACMP](Q12)** *step 5*
- **Continuous manufacturing (Q13)** *step 4*
- **Real world data (M14)** *step 1* etc…

Recent trend and challenges

- **Digital Transformation** [Clinical trials, etc.]
- **Stakeholders involvement, especially patients**
- **Quality related topics** [Lifecycle management, continuous manufacturing, etc.] etc…

ICH E17 Guideline for Multi-regional Clinical Trials (MRCT)

Early 1990s
- No guideline for using foreign clinical data

1998
- ICH E5: Ethnic Factors in the Acceptability of Foreign Clinical Data

2006~2007
- E5 Implementation Working Group Questions & Answers (R1)
- Basic Principles on Global Clinical Trials

2018
- ICH E17: General Principles for Planning and Design of Multi-Regional Clinical Trials
- ICH E17: Training Materials

Drug development in Japan

Local (only Japanese) clinical trials

Bridging strategies

A multi-regional trial for the purpose of bridging could be conducted in the context of a global development program

Japanese original principles on MRCTs

ICMRA (International Coalition of Medicines Regulatory Authorities)

https://www.pmda.go.jp/english/int-activities/int-harmony/icmra/0001.html

A voluntary, executive-level, strategic coordinating, advocacy and leadership entity of regulatory authorities (39 regulatory authorities) that work together to

- address current and emerging human medicine regulatory and safety challenges globally, strategically and in an on-going, transparent, authoritative and institutional manner
- provide direction for areas and activities common to many regulatory authorities' missions etc.

Chair
- Ms. Emer Cooke (EMA)

Vice Chair
- Dr. FUJIWARA (PMDA, Japan)
- Dr. John Skerritt (TGA, Australia)

Main Strategic Areas

1. **Innovation Project** (Utilization of method and results of horizon scanning):
   Japan serves as Co-chair

2. **Communications**: assigned as ICMRA PR
   Japan is responsible for website updates, and operation and maintenance management

ICMRA major activities for COVID-19 -workshops-

Global regulatory workshop on COVID-19 vaccine development

#1 March 18, 2020
#2 June 22, 2020

Global regulatory workshop on COVID-19 Real-World Evidence and Observational Studies

#1 April 6, 2020
#2 May 19, 2020
#3 July 22, 2020
#4 October 13, 2020
#5 January 25, 2021
#6 May 10, 2021
#7 May 20, 2022

Global regulatory workshop on COVID-19 therapeutic development

#1 April 2, 2020
#2 July 20, 2020

Vaccine Safety Collaboration Workshop

#1 January 13, 2021

Pregnancy and Lactation Workshop

#1 February 9, 2021

ICMRA-Industry Workshop on Enabling Manufacturing Capacity in the COVID-19 Pandemic

#1 July 7-8, 2021

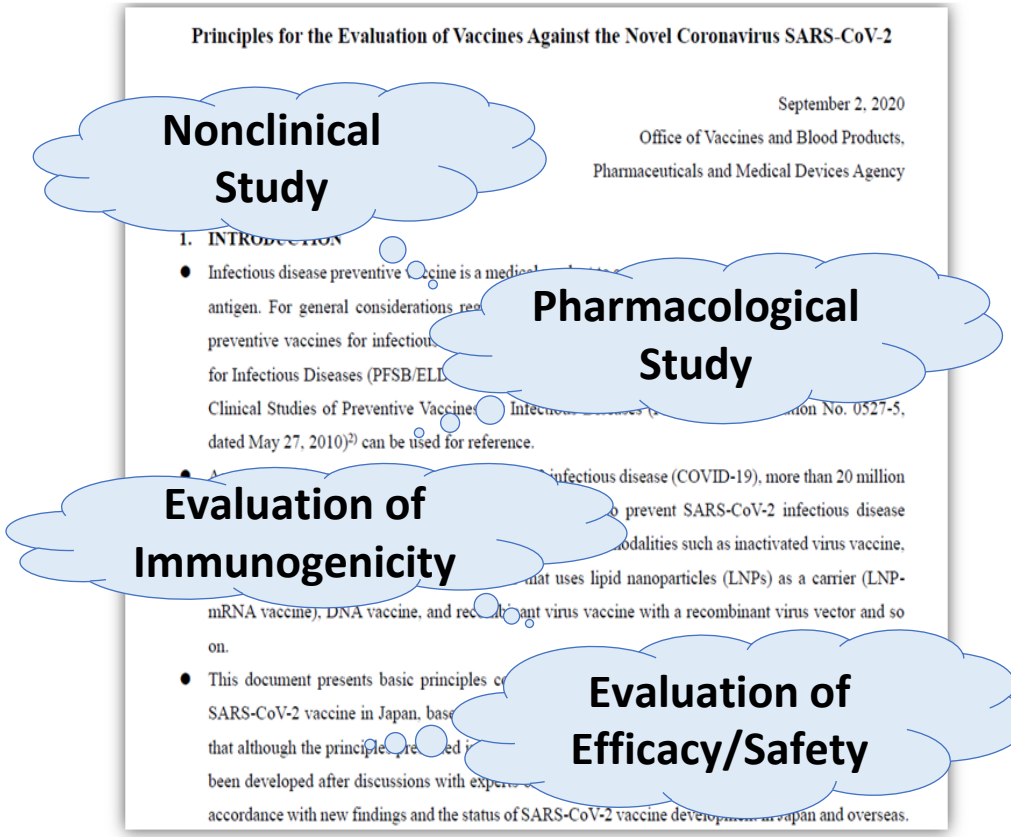
COVID-19 Virus Variants Workshop

#1 February 10, 2021
#2 June 24, 2021
#3 January 12, 2022
#4 June 30, 2022

Co-chairs:
Dr. FUJIWARA (PMDA)
Dr. June Raine (MHRA)

Japanese Guidance for the Evaluation of COVID-19 Vaccines based on the consensus of the ICMRA workshop

Principles for the Evaluation of Vaccines Against the Novel Coronavirus SARS-CoV-2 (PMDA)



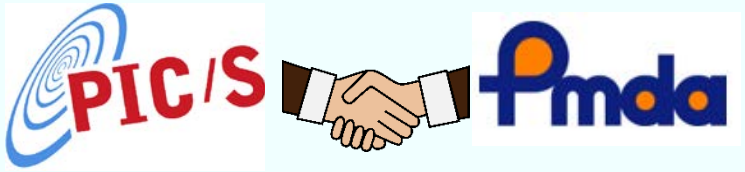
Published initially in Sep 2020

- Appendix 1, added in Apr 2021
  Evaluation of vaccines against variants
- Appendix 2, added in Jun 2021
  Ethical Considerations for Subjects in Placebo-Controlled Studies
- Appendix 3, added in Oct 2021
  Evaluation of the vaccines based on Immunogenicity
- Appendix 4, added in Jul 2022
  Immunogenicity-based evaluation of variant vaccines modified from parent vaccines and booster vaccines with new active ingredients

https://www.pmda.go.jp/english/about-pmda/0002.html

PIC/S (The Pharmaceutical Inspection Convention and Pharmaceutical Inspection Co-operation Scheme)

PIC/S Membership and Conduct of Internationally Standardized GMP Inspection



We are working on the following as a member of PIC/S.

- Maintain the relationship of mutual confidence with PIC/S member countries/regions in the field of GMP and improve quality of inspections
- Offer a framework to share information and experience
- Conduct mutual training
- Improve and harmonize the technical standards and procedures for testing
- Establish common guidelines
- Expand cooperative relationships with other regulatory authorities

Japan's PIC/S Activities

Joined the PIC/S members

Stage 0

2014

Held Expert Circle on Quality Risk Management (QRM) in Tokyo

Joined the Working Group on Annex 1

2015

Joined the Working Group on Advanced-Therapy Medicinal Products (WG-ATMP)

2016

Joined the Working Group on Data Integrity (WG-DI)

2017

Stage 1

Joined the Working Group on Annex 2

2018

Joined Sub Committee on Training (SC-T)

2019

Joined the Expert Circle on Quality Risk Management

2020

Stage 2

Held PIC/S Committee Meeting and Seminar 2019 in Toyama

Joined the Working Group on Control of Cross-Contamination in Shared Facilities (WG-CCCSF)

Joined the Working Group on ICH Q12 Training Material

2021

Joined the Working Group on Remote Assessment

2022

Hosted the Sub Committee on Communication (SC-COM)

Stage 3

Joined the Executive Bureau

PDG (Pharmacopoeial Discussion Group)

- The Pharmacopeial Discussion Group (PDG) was formed in 1989
- Members are representatives from the Japanese Pharmacopoeia, the European Pharmacopoeia and the U.S. Pharmacopeia
- The purpose is harmonizing pharmacopeial standards (excipient monographs and selected general chapters)
- Closely collaboration with ICH and tasked with the Maintenance of 14 annexes of ICH Q4B

独立行政法人
医薬品医療機器総合機構
Pharmaceuticals and Medical Devices Agency

Press Release

PHARAMACOPOEIAL DISCUSSION GROUP AHIEVEMENTS

The Pharmacopoeial Discussion Group (PDG), which brings together the European Pharmacopoeia (Ph. Eur.), the Japanese Pharmacopoeia (JP) and the United States Pharmacopeia (USP), with the World Health Organization (WHO) as observer held its annual autumn meeting from 18 to 21 October 2022. Due to the COVID-19 pandemic, the meeting was again organized through videoconference. For the first time, the Indian Pharmacopoeia Commission (IPC) joined the meeting as a pilot participant in the PDG pilot for global expansion.

The PDG Members were delighted to welcome the IPC. The IPC introduced its organizational structure, its pharmacopoeia and its plan for harmonising with the PDG. This was a landmark meeting in the PDG's 33-year history since the PDG welcomed an additional pharmacopoeia, marking the launch of a one-year pilot for expansion of its membership, as announced in an earlier press release (link). The lessons learned from this pilot will be used to further adjust and refine the group's working methods and will identify any changes necessary to ensure that the PDG continues to perform efficiently at the end of the pilot.

One of the primary outcomes of the meeting was the consensus reached on a proof-of-concept study for the maintenance of the ICH Q4B annexes (link). Following exchanges with the four other pharmacopoeias involving the discussion at the PDG interim videoconferences on 15 and 28 March 2022 (link), revised drafts of three selected Q4B annexes (Annex 6: Uniformity of Dosage Units, Annex 7: Dissolution and Annex 8: Sterility) had been prepared. Based on these drafts, PDG finalized the report with recommendations for some key questions, which had been raised in this proof-of-concept study. The PDG reported the conclusions of this study and recommendations for next steps to the ICH Assembly in November 2022.

https://www.pmda.go.jp/files/000249673.pdf

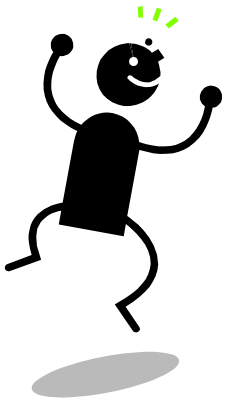
In Sep 2022, PDG invited the Indian Pharmacopoeia Commission (IPC) as a participant in the PDG pilot for global expansion.

Utilization of Japanese Pharmacopoeia (JP)

—Streamline assessment process of Marketing Authorization —

- Specifications are standardized among manufacturers.
- When General Tests and test methods specified in Monographs are used in the submission for drug applications in Japan, they are considered as validated methods, resulting in no requirement of the validation data, in general.

Taking less time for review and evaluation.



Five Principles for Basic Principles for JP revision

1. Including all drugs which are important from the viewpoint of health care and medical treatment
2. Making qualitative improvements by introducing the latest science and technology
3. Further promoting internationalization in response to globalization of drug market
4. Making prompt partial revision as necessary and facilitating smooth administrative operation
5. Ensuring transparency regarding the revision and disseminating the JP to the public

Establishment of Japanese Pharmacopoeia (JP)

Original drugs (new drugs)

widely used in public and well-established

Patent term

Reexamination period to verify efficacy and safety

Generic drugs | Generic drugs | Original drugs | Generic drugs | Generic drugs

Preparation of drafts

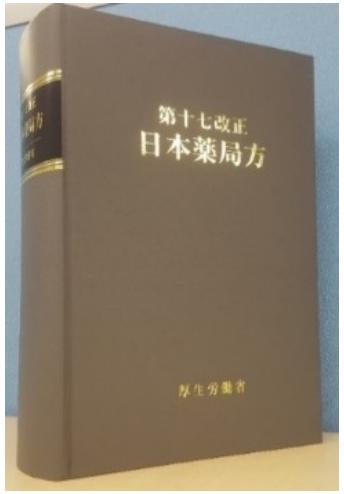
mainly by the manufacture of the original drug

Public Comment

Listing in the JP

Standardization by the JP

Ideal form of the drug product



Asia Training Center for Pharmaceuticals and Medical Devices Regulatory Affairs (PMDA-ATC)

- Established in April, 2016.
- Endorsed as Centers of Excellence (CoE) of APEC-LSIF-RHSC.
- Promote capacity building and human resource development through training seminars for Asian regulators.

Seminars/Webinars

FY2022 (April 2022 – March 2023)

	Contents	Date
1	Quality Control (Herbal Medicine)	August 23-25, 2022
2	Pediatric Review	September 12-15, 2022
3	Good Manufacturing Practice (GMP)	October 25-26, 2022
4	Good Registration Management	September 13, 2022
5	Medical Devices Review I	November 14-16, 2022
6	Medical Devices Review II	November 28-30, 2022
7	Pharmaceuticals Review	December 6-10, 2022
8	Multi-Regional Clinical Trial (MRCT)	January 16-19, 2023
9	Pharmacovigilance	February 6-9, 2023

https://www.pmda.go.jp/english/int-activities/training-center/0004.html

E-learning (YouTube)

Over 40 contents are available on the PMDA channel

#	Category	N
1	Review	17
2	Safety	4
3	Relief	3
4	Medical Device	6
5	GxP	7
6	PMDA Efforts	9

https://www.pmda.go.jp/english/int-activities/training-center/0003.html

Working as “Team Asia” toward Asian people