Japanese Pharmacopoeia's Challenge to the Globalization

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1. Introduction

Introduction: History of JP Edition

Edition	Date of publication	Number of monographs
JP 1	1886.6.25	468
↓	↓	↓
JP 16	2011.3.31	1764
Suppl. I	2012.9.27	1837
Partial rev.	2013.5.31	1837
Suppl. II	2014.2.28	1896
↓	↓	↓
JP 17	2016.2	1962

Introduction: Legal Status of JP

- Article 2 -

Act on Securing Quality, Efficacy and Safety of Pharmaceuticals, Medical Devices, Regenerative and Cellular Therapy Products, Gene Therapy Products, and Cosmetics

The term “drug” in this Law refers to the following items:

1. Items recognized in the **Japanese Pharmacopoeia.**
2. Items (excluding quasi-drugs or cellular and tissue-based products) which are intended for use in the diagnosis, cure or prevention of disease in humans or animals, and which are not equipment or instruments.
3. Items (excluding quasi-drugs or cosmetics) which are intended to affect the structure or functions of the body of humans or animals, and which are not equipment or instruments.

Introduction: Legal Status of JP

- Article 56 -

Act on Securing Quality, Efficacy and Safety of Pharmaceuticals, Medical Devices, Regenerative and Cellular Therapy Products, Gene Therapy Products, and Cosmetics

No drug which comes under any of the following items shall be sold or given, or manufactured, imported, stored, or exhibited for the purpose of sale or giving:

1. The quality or properties are not in conformity with the standards established by **Japanese Pharmacopoeia (JP)**

Japanese Pharmacopoeia Chapters

- Main Body (Mandatory part)
  1. General Notices - general rules for drafting, interpreting, and utilizing the Japanese Pharmacopoeia
  2. General Rules for Crude Drugs - general rules for drafting, interpreting, and utilizing the official monographs of crude drugs
  3. General Rules for Pharmaceutical dosage forms - common rules and interpretation about preparations
  4. General Tests, Processes and Apparatus - highly common test methods
  5. Official Monographs - specifications and test methods per drug
  6. Infrared Reference Spectra and Ultraviolet-visible Reference Spectra
- General Information

Structure of JP development and implementation

Pharmaceutical Affairs and Food Sanitation Council (PAFSC)

NIID

PMRJ JPRS Lab

registration

Notice

Ministry of Health, Labour and Welfare

Commission

Report

Development of JP

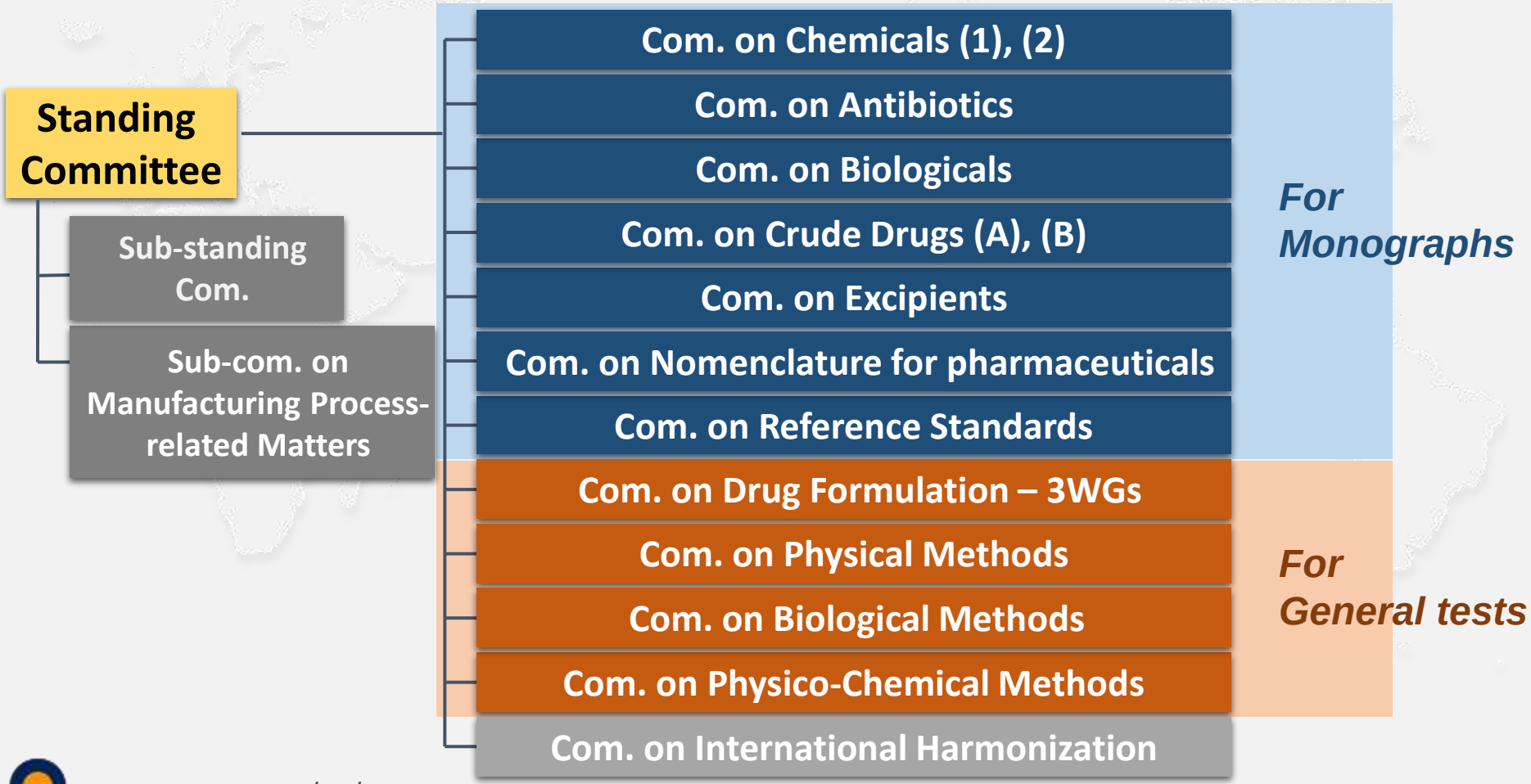
JP Secretariat

JP Expert Committees

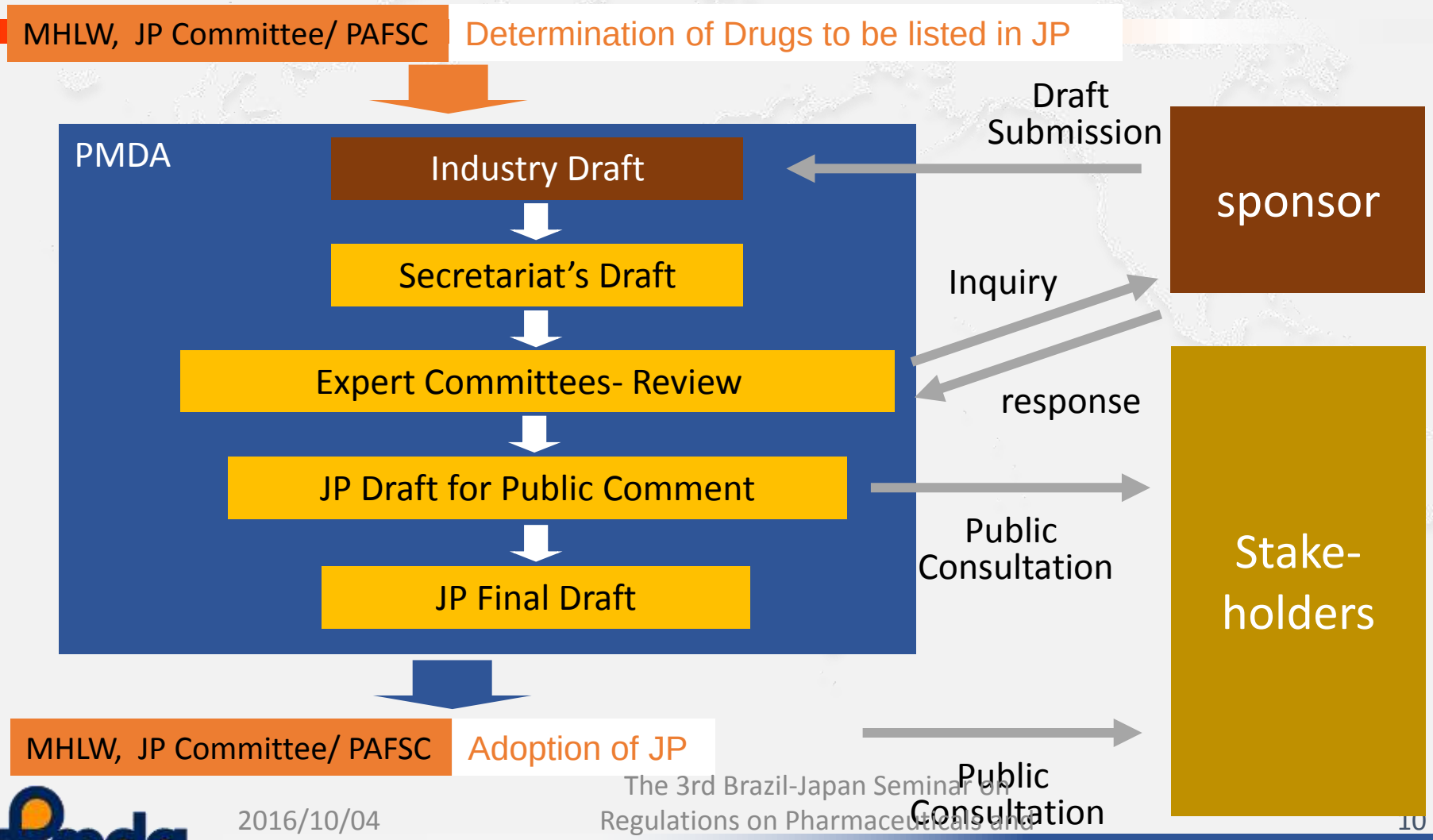
JP

Reference Standards

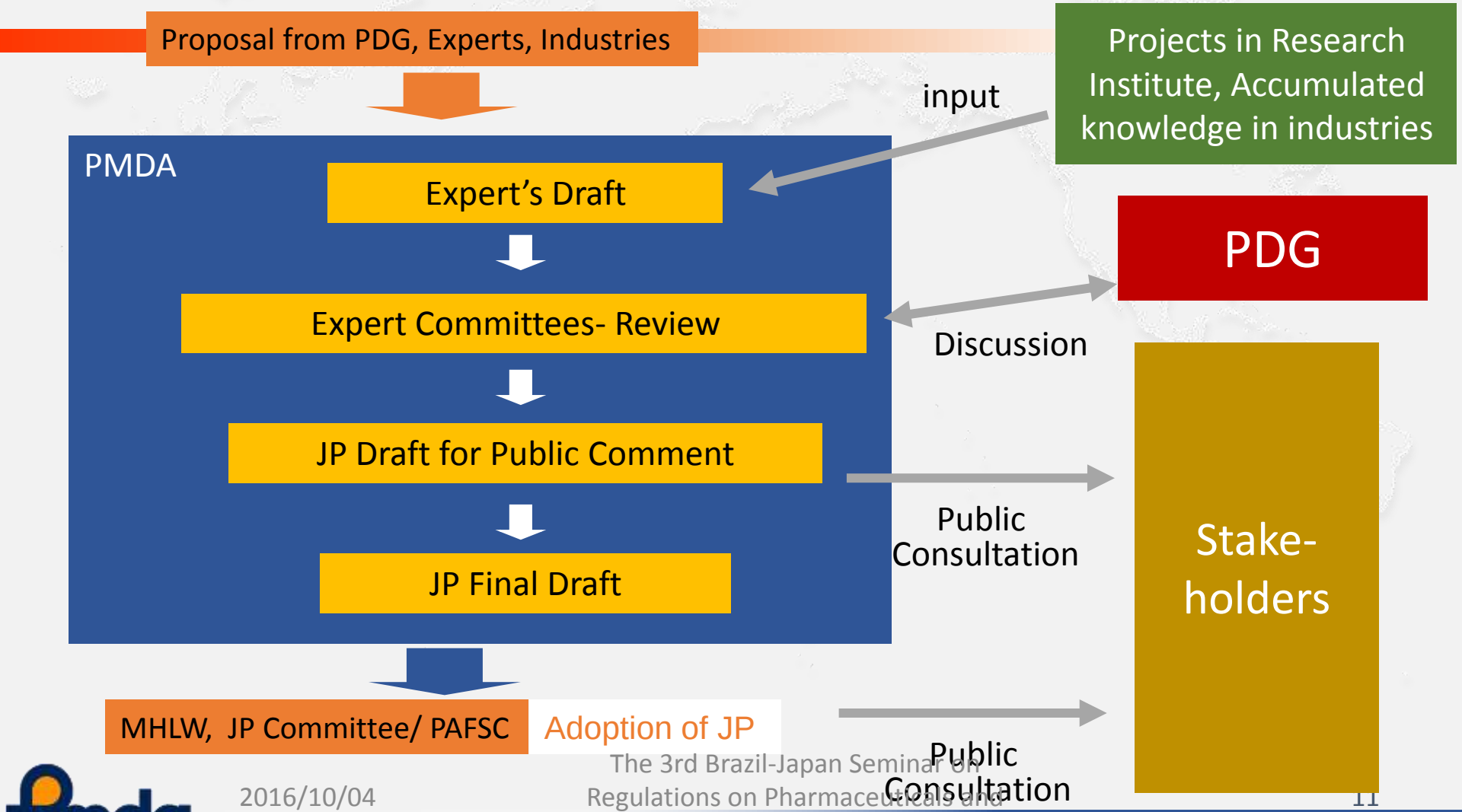
Organization of JP Expert Committees



Methodology of developing JP monographs

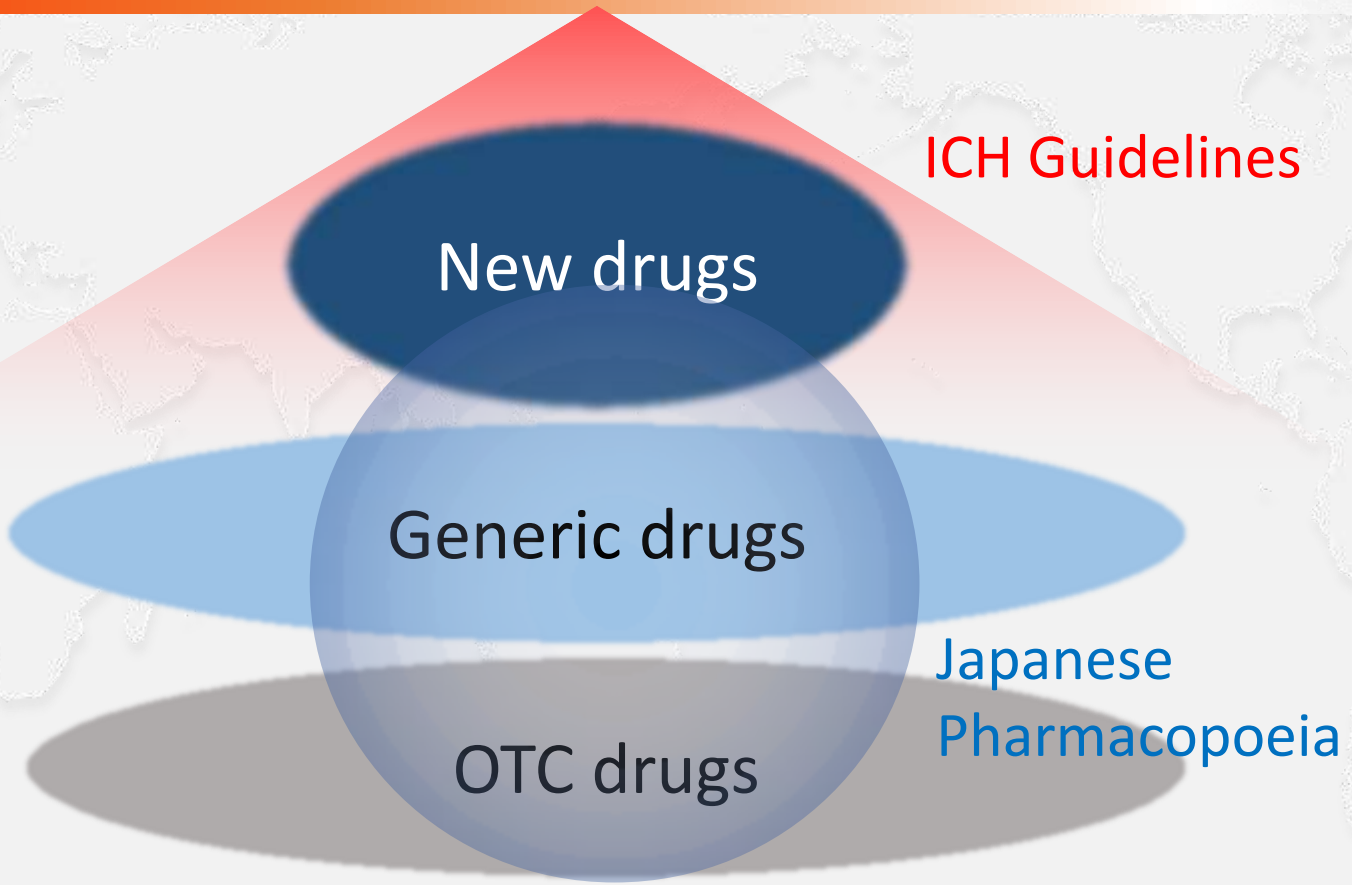


Methodology of developing JP General tests

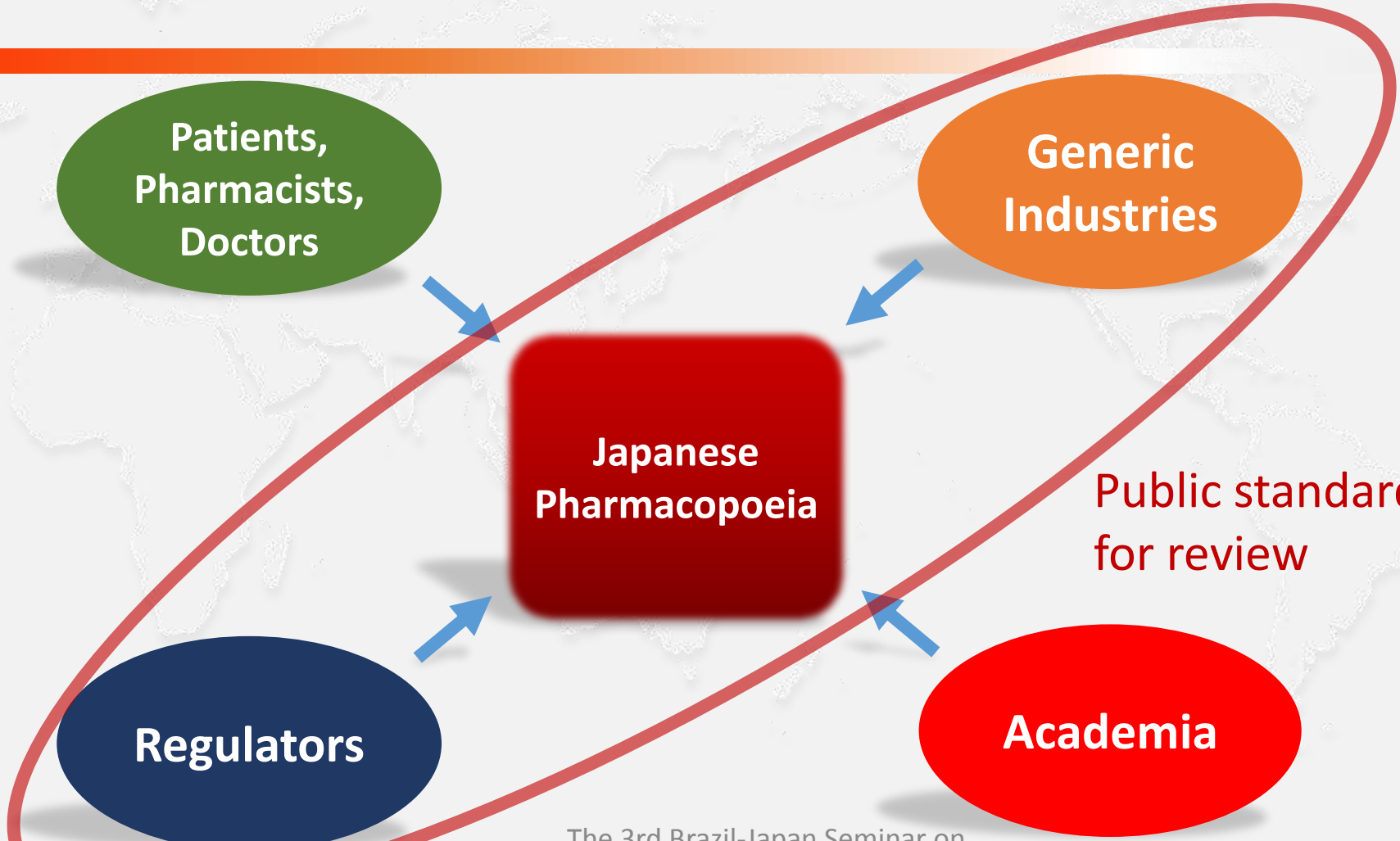


2. Regulatory Role of JP

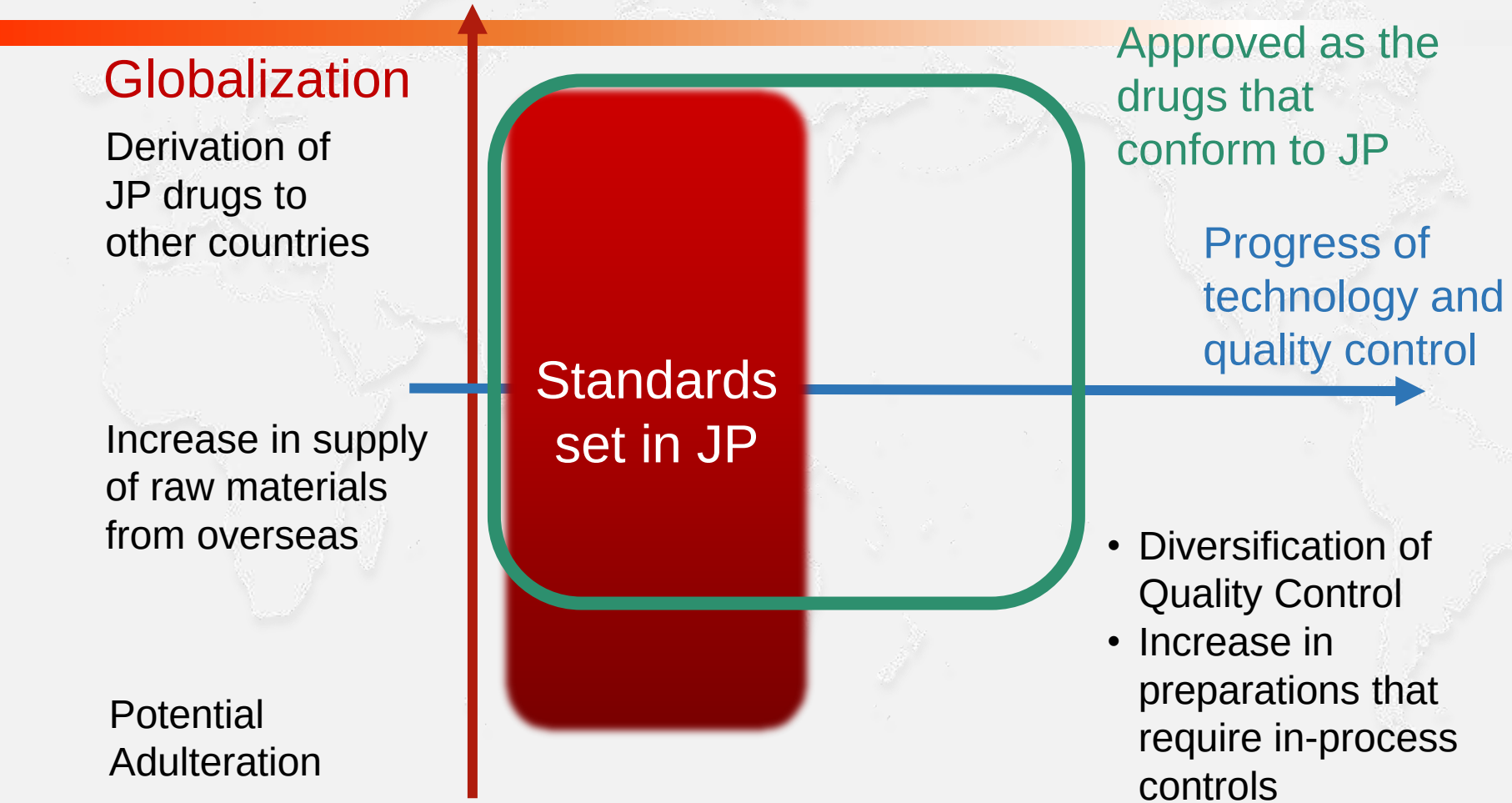
Guidelines and standards in Japanese Regulatory System



For Regulation of Generic Drugs



Role of Japanese Pharmacopoeia in the expanding regulatory scope



3. New Topics in JP

Major Revision Points in JP17

- New policies of specification setting of impurities in JP monographs
- New articles about production and quality control
- Introduction of new headings of “Manufacture” and “Potential adulteration”
- Comprehensive regulation of residual solvents.
- Revision of Containers and Packages
- Revision related to the Biological methods

New policies of specification setting of impurities in JP monographs

- **The purity test using the reference standards of impurities**
  - Chromatographic method using the reference standards of impurities will be adapted in the Purity test.
- **The second test method for the purity test**
  - For the drugs manufactured by a different chemical syntheses and thus having a different impurity profile, the Second Test Method may be adopted in the Purity test.

New articles about production and quality control

- **Following articles are to be adopted in General Information**
  - "Basic concepts of quality assurance of drug substances and drug products", which is based on ICH-Q6A and Q6B philosophy
  - "Basic concepts of quality risk managements", which is based on ICH-Q9 philosophy

Revision regarding the Reference Standards

- **Adoption of a new concept for Reference Standards were discussed, considering the consistency with other pharmacopoeias**
  - Requirements to set the Reference Standards used for the tests other than the Assay in the Official Monograph
  - Requirements for the specification of the Reference Standards used for non-Assay tests
  - Consideration of influence on the distributors of Reference Standards
- **Major Revision of General Test, <9.01> Reference Standards**

4. New Strategy of JP

The Latest Strategic movement of JP

JP17th edition (Japanese version) was published and legally noticed on 7th March.

- The draft basic principal for JP18th revision had been discussed by cross-sectional expert committees in PMDA.
- The principal was deliberated by Pharmaceutical Affairs and Food Sanitation Council in MHLW and finally disclosed for public comments from 19th Aug to 18th Sept.

Basic Principals for Drafting of JP 18th Edition -Five pillars for JP revision-

1. Including all the drugs essential for health care and medical treatment
2. Improving quality by proactive introduction of latest science and technology
3. Further progress of internationalization to fit to the globalization of drug market
4. Timely updating and revising as necessary and facilitating smooth administrative operation
5. Ensuring transparency in the process of revisions and disseminating JP

PMDA International Strategic Plan 2015
Vision II: To maximize the common health benefits to other countries/regions

Expediting the global utilization of the Japanese Pharmacopoeia

- Further expedite harmonization of the JP, USP and EP through the activities of the PDG.
- Contribute to improving quality of pharmaceuticals that are globally distributed, by proactively incorporating in the JP the concept of quality assurance based on cutting-edge science, and by promoting JP as one of the reference pharmacopoeia in other countries/regions.

Regulatory Science Initiative of MHLW states promotion of positioning of JP as one of the reference pharmacopoeia in Asian countries.

Further progress of internationalization to fit to the globalization of drug market

1. JP will contribute to the international compendial movement for harmonization including WHO.
2. The international harmonization of pharmaceutical excipients and general tests should be promoted through the Pharmacopoeial Discussion Group (PDG) and the harmonized items should be swiftly implemented in the JP.
3. The approaches to promote internationalization of the JP especially in Asia should be considered.
4. JP should positively support the harmonization activities for crude drugs in Asia through the crud drug harmonization forum.
5. Prompt publication and user-friendly contents of the English version of JP should be considered for world-wide users.
6. Training course of JP for world-wide regulators should be examined.

Improving quality by proactive introduction of latest science and technology

- Roadmap for implementation of ICH-Q3D in JP monographs is to be developed.
- The policy for developing monographs and test methods for biotechnology products is to be discussed.
- Appropriate and flexible specifications in the monographs by using heading “Manufacture” or “Potential adulteration” etc.

5. Internationalization of JP

International Meetings of World Pharmacopoeias

- Primary Global Pharmacopoeial Initiative
- International Arena of world pharmacopoeias for information exchange and cooperation
- The objective of the WHO Good Pharmacopoeial Practices (GPhP) guidance is to harmonize approaches and policies in establishing pharmacopoeial standards.
- It is envisaged that GPhP will:

  strengthen global pharmacopoeial cooperation;

  increase transparency on how pharmacopoeial standards are developed and maintained; and

  improve cooperation between pharmacopoeial authorities and stakeholders (e.g. regulators, industry).

International Meetings of World Pharmacopoeias

- 7th International Meeting of World Pharmacopoeias was co-hosted by WHO & JP in Tokyo Japan on 13-14 September, 2016
- Chapters for Compounded preparation, Herbal medicines, and Glossay were discussed and the participants reached agreement in principle on how to proceed these items for finalizing.
- Actions and proposals for the future meeting were also discussed.
- 8th Meeting will be co-hosted by WHO & Brazilian Farmacopoeia in 2017

Pharmacopoeial Discussion Group (PDG)

- European Pharmacopoeia (EP),United States pharmacopeia (USP) and Japanese Pharmacopoeia (JP) participate.
- It was launched in 1989. WHO started participating as an observer in 2001. It meets twice per year.
- Harmonization is carried out retrospectively for existing excipient monographs and general chapters or prospectively for new monographs or chapters.

	Harmonized Items (under revision)	In progress
General Chapters	29	7
Monographs	49	18

PDG Activities

PDG works to harmonize important general chapters such as physicochemical tests, tests for dosage forms, and tests for biotechnological products and major excipients monographs.

- To reduce manufacturer's burden of performing analytical procedures in different ways, using different acceptance criteria
- To unify specification of excipients that can be used for a number of drug products
- To maintain an optimal level of science consistent with protection of public health

Further progress of PDG Activities is expected

Harmonization item	Stage
Color (instrumental method)	4
Conductivity	4
Elemental Impurities	3
Inhalation	4
Uniformity of Delivered Dose of Inhalations	2
Chromatography	3
Dynamic Light Scattering	3
Protein Determination (Rev. 1)	4
Peptide Mapping (Rev. 1)	4

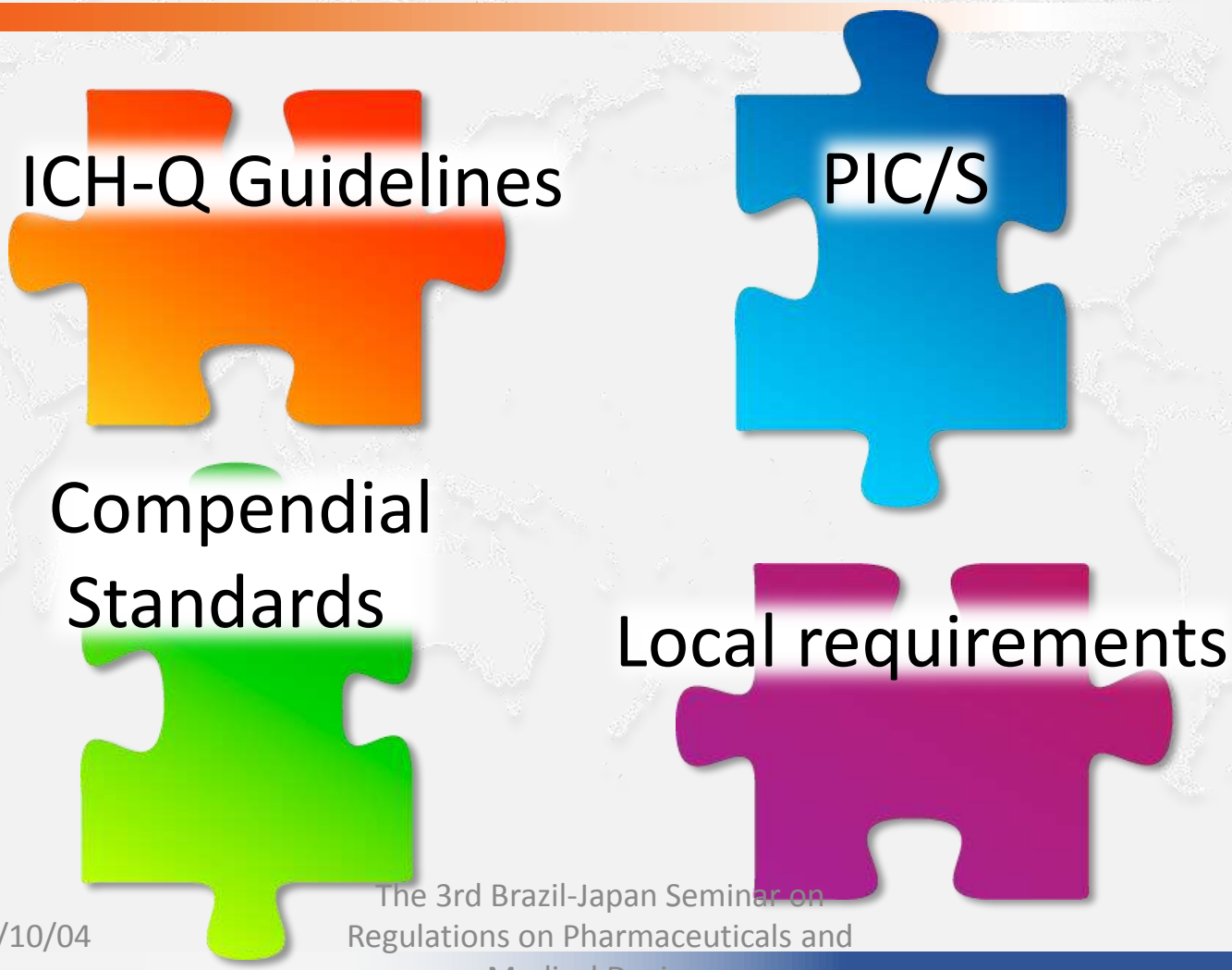
The harmonization of remaining PDG general test items are highly expected by world-wide users.

Further progress of PDG Activities is expected

- 49 of the 67 excipient monographs on the current work program have been harmonized.
- Five new items, Isostearyl alcohol, Myristyl myristate, Polysorbate 65, Sodium cetyl sulfate and Calcium silicate originated from JP-USP bilateral harmonization program, are added to the PDG work program.
- With the exception of the Calcium silicate (major revision for USP), these items will be the first excipient monographs to be elaborated within the PDG using a prospective approach.

6. Expectation for collaboration with Brazilian Farmacopoeia

To convergence the regulatory action referring the compendial standards



Summary

- Considering globalization of drug supply chain and progress and diversification of quality control, there is a need to change the quality of Japanese Pharmacopoeia (JP) as well as the JP's position in the reviews of marketing applications.
- Keeping qualitative fulfillment, JP will proactively make international development.
- To convergence the regulation for drug approval, basal concepts of the review and evaluation process of drugs referring the JP should be shared with Brazilian Farmacopoeia.