JP future perspectives

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USP-MHLW/PMDA Joint Workshop 2024

Basic Principles for Preparation of JP19

-Five Principles for JP revision-

1. Enriching monographs by prioritizing inclusion of drugs which are important in healthcare
2. Making qualitative improvement by introducing the latest science and technology
3. Promoting further 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 throughout Japan and the rest of the world

Summary of JP18-2 (June 28, 2024)

New General Tests and General Information

	Number
General Tests	1
General Information	6

New Monographs

Type	Number
Chemicals (Substances, Products)	12 (6, 6)
Crude Drugs (Herbals)	1
Total	13

JP18
on June 7, 2021

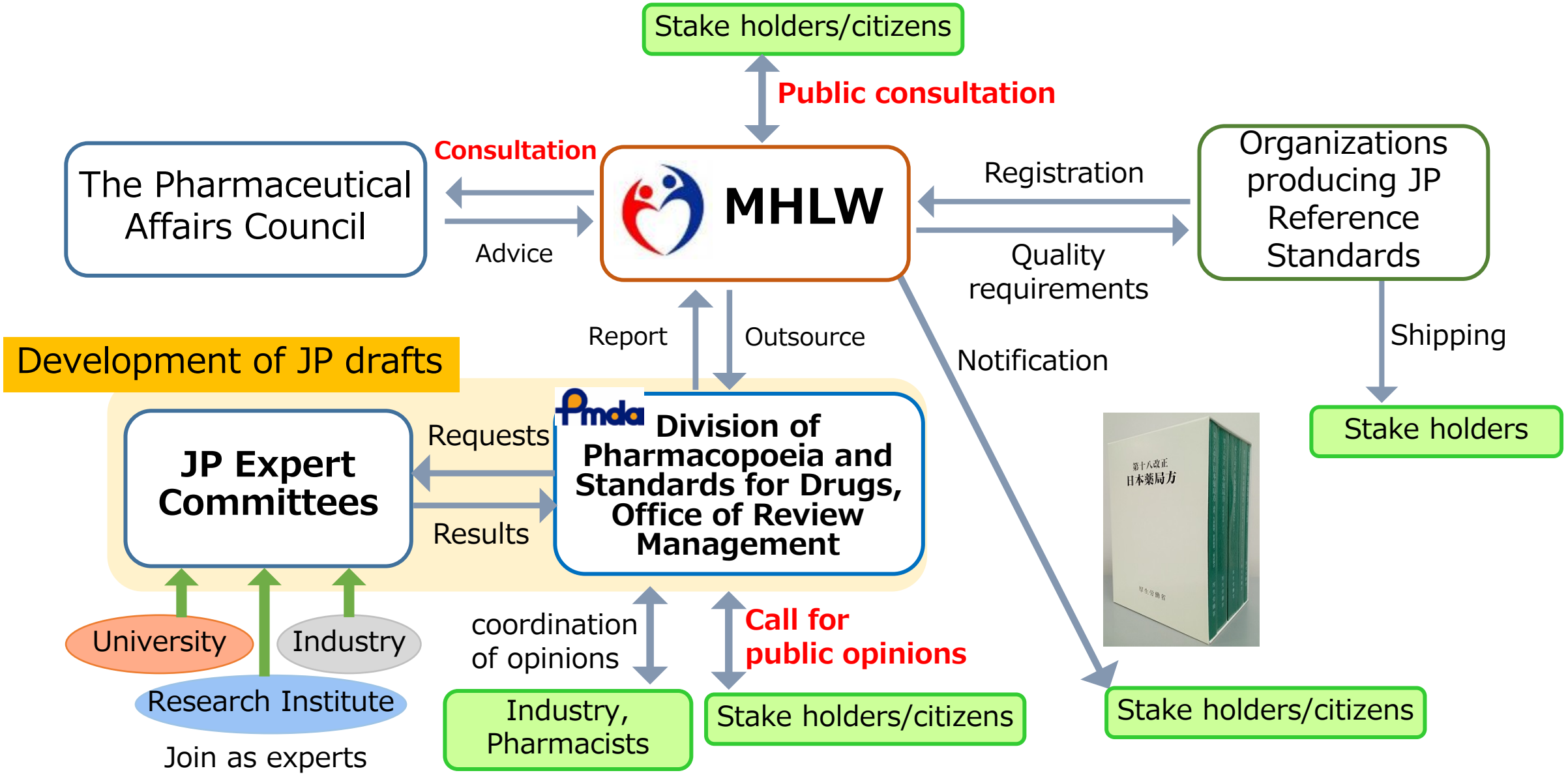
JP18-1
on December 12, 2022

JP18-2
on June 28, 2024

- **Basic Principles for Preparation of JP19 in October 2021**
- **Guideline for drafting JP19 in March 2022**

JP19
in Spring, 2026 (planned)

For developing/revising Japanese Pharmacopoeia



General monograph of monoclonal antibodies

General Information: Basic Concept of the Quality Control on Biotechnological Products (Biopharmaceuticals) <*G3-1-180*>

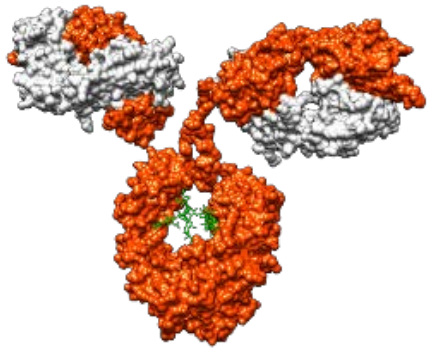
(1) Characteristics and control strategy of monoclonal antibodies (mAbs)

Brief overview of mAbs

Characterization of mAbs

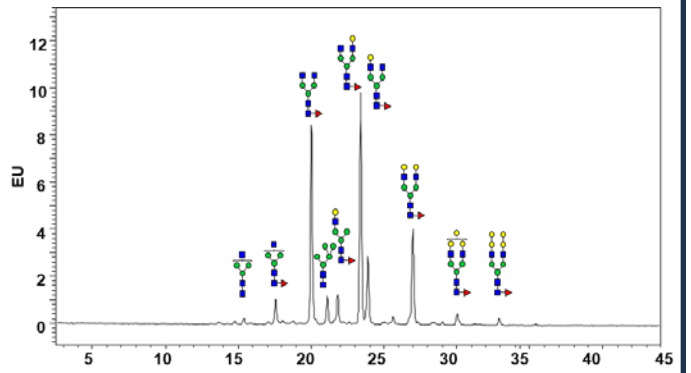
Risk assessment and typical critical quality attributes of mAbs

Control strategy of mAbs
- Raw material control
- Process control
- In-process tests
- **Specifications**



The general monograph is under preparation.

(2) Examples of specifications



Origin
Manufacture
Description
Identification
Charge variants
Glycosylation profile
Purity (1) aggregates
Purity (2) low molecular weight species
Biological activity (1) antigen binding
Biological activity (2) FcγR IIIa activation
Assay
Storage
Reagents and test solutions

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Introducing the latest science and technology

Development and update of general tests with latest knowledge and analytical technology

JP18-1

- 2.27 **Near Infrared Spectrometry**
- 2.28 **Circular Dichroism Spectroscopy**

Development of general information on state of the art analytical methodology

JP18-1

- Control Strategies and Change Control Concepts at Each Stage of **Chromatography Lifecycle** (Change Control in Chromatography Lifecycle) 〈*G1-5-181*〉
- Measurement of Powder Flow Properties by **Shear Cell Methods** 〈*G2-5-181*〉

JP18-2

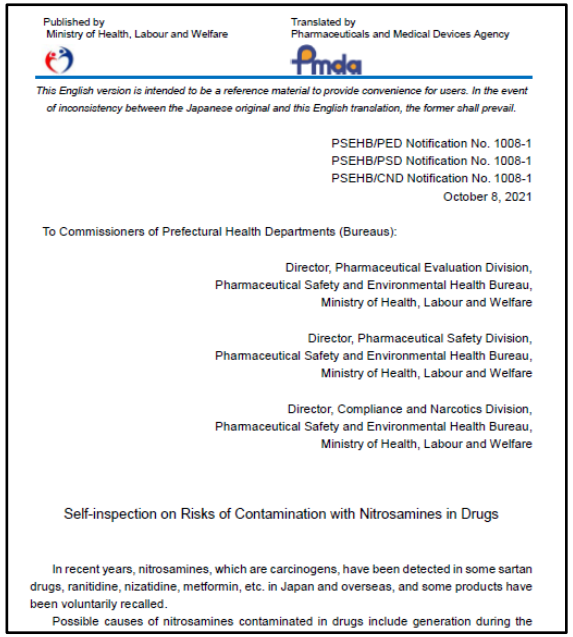
- Analyses of Size and Morphology of Nanoparticles by **Atomic Force Microscope** 〈*G1-9-182*〉
- Flow Cytometry 〈*G3-16-182*〉
- Evaluation of Insoluble Particulates in Biotechnological Products (Biopharmaceuticals) Drug Substances/Drug Products by **Flow Imaging Method** 〈*G3-17-182*〉

JP19 (expected)

- Points to Consider in Suitability Testing, etc. of Microbial Tests 〈*G4-12-190*〉
- **Reference NMR spectra based on ^{1}H spin information** and their application to Japanese Pharmacopoeia reagents <*G5-9-190*>
- **Uniformity of Delivered Dose** of Nasal Preparations

About nitrosamine impurities

Notification No. 1008-1: Self-inspection on Risks of Contamination with Nitrosamines in Drugs



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This English version is intended to be a reference material to provide convenience for users. In the event of inconsistency between the Japanese original and this English translation, the former shall prevail.

PSEHB/PED Notification No. 1008-1
PSEHB/PSD Notification No. 1008-1
PSEHB/CND Notification No. 1008-1
October 8, 2021

To Commissioners of Prefectural Health Departments (Bureaus):

Director, Pharmaceutical Evaluation Division,
Pharmaceutical Safety and Environmental Health Bureau,
Ministry of Health, Labour and Welfare

Director, Pharmaceutical Safety Division,
Pharmaceutical Safety and Environmental Health Bureau,
Ministry of Health, Labour and Welfare

Director, Compliance and Narcotics Division,
Pharmaceutical Safety and Environmental Health Bureau,
Ministry of Health, Labour and Welfare

Self-inspection on Risks of Contamination with Nitrosamines in Drugs

In recent years, nitrosamines, which are carcinogens, have been detected in some sartan drugs, ranitidine, nizatidine, metformin, etc. in Japan and overseas, and some products have been voluntarily recalled.
Possible causes of nitrosamines contaminated in drugs include generation during the

- Published by Pharmaceutical Safety and Environmental Health Bureau, MHLW
  - Director, Pharmaceutical Evaluation Division,
  - Director, Pharmaceutical Safety Division,
  - Director, Compliance and Narcotics Division,
- Published date: Oct 8, 2021

Items to be confirmed, implementation deadline, etc.

(The procedures for self-inspection of **the marketed products**)

① Risk evaluation by the company
- To evaluate the risk of contamination
- with referring to the known root causes

✓ Deadline: April 30, 2023

② Measurement of the amount of nitrosamines
- In an appropriate number of lots

✓ When the result of exceeding the limit, report to MHLW

③ Risk reduction
- Setting an acceptance criteria
- Changing the manufacturing process
- Regulatory action
  - Application for approval of partial change
  - Notification of minor change

✓ Deadline: August 1, 2025

About nitrosamine impurities

JP is considering to include ICH M7

The Basic Principles for the 19th Edition of the JP states that "ICH-M7 Guidelines should also be considered" in the ⑥ Improvement of the impurity management in light of international trends of the (2) **Making qualitative improvement by introducing the latest science and technologies**.
We established "**ICH M7 inclusion working group**" under the General Committee to discuss the incorporation of this guideline into the JP.

We have now been discussing what and where to include the ICH M7 guideline into JP

Related topic: ICH Fukuoka meeting (June 2024)

An Addendum to the Multidisciplinary Guideline M7 on "Assessment and Control of DNA Reactive (mutagenic) Impurities in Pharmaceuticals to Limit Potential Carcinogenic Risk" to address **safety assessment and establishment of appropriate controls for nitrosamine impurities through a staged approach**, leveraging the Formal ICH Procedure, as well as to **develop a harmonised set of acceptable intakes (AIs)** leveraging the M7 Maintenance Procedure.

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Promoting further internationalization for globalization of drug market

Prompt release of the JP English version is the basis for internationalization and international cooperation

JP: English version release

	Japanese version	English version	Days involved
JP17	March 7, 2016	September 8, 2016	**190**
JP17-1	December 1, 2017	September 13, 2018	**286**
JP17-2	June 28, 2019	February 21, 2020	**238**
JP18	June 7, 2021	March 14, 2022	**280**
JP18-1	December 12, 2022	June 23, 2023	**193**
JP18-2	June 28, 2024	In progress	**?**

Guideline for drafting monographs for the Japanese Pharmacopoeia, 19th edition

Manual for drafting monographs of chemical drugs, biologicals and crude drugs

English version has not been released from PMDA, but draft version will be publicized soon

Promoting further internationalization for globalization of drug market

MHLW(2023.12.11)

Meeting of stakeholders on measures to ensure stable supply of prescription drugs

Further to promote international harmonization with other pharmacopoeias through the PDG activities and others.

Pilot activities for monographs

Bilateral harmonization with USP

2023.10~

Dapagliflozin Propylene Glycolate Hydrate its tablet

Bilateral harmonization with EP

2024.4~

Macitentan its tablet

Expedited deliberations on revisions to the JP by the shortages in prescription drug supply (Aug. 1, 2024, MHLW notification)

For prescription drugs with concerns on stable supply in Japan (including condition that it is possible to ensure quality without need to change manufacturing sites, manufacturing methods, etc.)

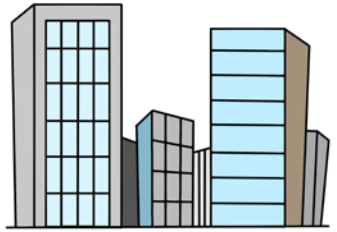
Can expediting deliber-ations on the revision of JP to achieve international harmonization

Project for promotion of international harmonization of pharmacopoeias (2023-2024)

To ensure **a stable supply of pharmaceuticals by promoting international harmonization of pharmacopoeias** and streamlining procurement of drug substances, **necessary facilities and systems are established in National Institute of Health Sciences (NIHS)** to make/modify test methods for international harmonization and to enable data to be obtained.

Spending delegation from MHLW to NIHS (total 500 million yen)

Pharmaceutical company



Depends on applicant's data

MHLW

Specification test data

JP

<Monographs>

Promotion of international harmonization

NIHS

Spending delegation for test apparatuses

Establish a system for conducting tests necessary for international harmonization

Stable supply of pharmaceuticals

Current plan for JP20 and perspectives

JP19
in Spring, 2026 (planned)

JP19-1
in Autumn, 2027 (planned)

JP19-2
in Spring, 2029 (planned)

JP20
in Spring, 2031 (planned)

- **Basic Principles for Preparation of JP20 in Autumn 2026**
  - **Started to discuss in each committee**
  - **Each committee will select several important topics for next 5 years**
  - **Main stream of the current JP19 version would be held, but more internationalization would be included** (My personal opinion)
- **Guideline for drafting JP20 in Spring 2027**
  - **The current version is the fruit of past wisdom and know-how in JP**
  - **Main contents of the current version would be held, but more internationalized aspects and flexibility would be included** (My personal opinion)
  - **In addition, required (especially scientifically) and recommended parts could be shown separately** (My personal opinion)

Potential future discussion/collaboration with USP

1) Basic stance on the determination of specification ranges scientifically (Contents, System suitability tests of assay and impurities, etc.)

2) Collaborative investigation of HPLC and TLC methods to reduce hazardous chemicals (Development of alternative methods) for promotion of environmental footprint.

3) Harmonization of General Chapter (tests) on biological products such as monoclonal antibodies, and also general monographs

4) Monographs and General Chapters (tests) of new modality drugs (antibody-drug conjugates, oligonucleotide, peptide with unnatural structures, etc.)

5) Inter-collaborative validation of new analytical methods for future inclusion to pharmacopoeias (with NIHS)

6) Up-to-date discussion about the impacts of ICH Q6 revisions on pharmacopoeias (especially, after revised draft guideline will be publicized)

Thank you for your attention!!