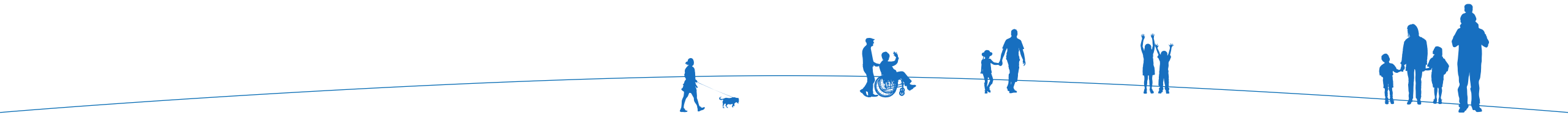
PSJ 公益社団法人 日本薬学会
The Pharmaceutical Society of Japan

PMDA
Making everyone's lives brighter together

Regulatory approach to promote orphan drug development in Japan

Akiko MASE
Principal Reviewer, Office of New Drug I
Pharmaceuticals and Medical Devices Agency, Japan



Disclaimer

The views and opinions expressed in the following slides are those of the individual presenter and should not be attributed to the organization with which the presenter is employed.

Today's topics

- Orphan drug designation system in Japan
- Recent regulatory efforts to further promote orphan drug development in Japan

PMDA
Making everyone's lives brighter together

- **Orphan drug designation system in Japan**
- Recent regulatory efforts to further promote orphan drug development in Japan

PMDA
Making everyone's lives brighter together

Legal basis of orphan drug designation

Legislation etc.	Corresponding part	Description
PMD Act[1)]	Article 77-2	Overview of orphan drug designation system
Regulation for Enforcement of PMD Act[2)]	Article 251	Upper Limit on the Number of Patients
PSB/PED Notification No. 0116-1[3)]	All	Details of designation criteria
Administrative Notice[4)]	All	Q&A for designation of orphan Drugs etc.

1) Act on Securing Quality, Efficacy and Safety of Products Including Pharmaceuticals and Medical Devices (https://www.japaneselawtranslation.go.jp/ja/laws/view/3213/en)
2) Regulation of Enforcement of the Act on Securing Quality, Efficacy and Safety of Products Including Pharmaceuticals and Medical Devices (https://www.japaneselawtranslation.go.jp/ja/laws/view/3215/en)
3) https://www.pmda.go.jp/files/000268408.pdf
4) https://www.pmda.go.jp/files/000268407.pdf

PMDA
Making everyone's lives brighter together

Orphan drugs – designation system

Aim

✓ To promote R&D on products for rare diseases, aiming to provide the people with the safe and effective medicines/medical devices as early as possible

Designation Criteria

1. Number of subjects (that any of the followings is satisfied)
   - Less than 50,000* in Japan *Equivalent to 0.04% of the Japanese population
   - The target disease is one of the designated intractable disease (Nan-byo)
2. Medical needs
   - For serious diseases with high medical needs
3. Possibility of development

Incentives

**National Institutes of Biomedical Innovation, Health and Nutrition

Grant-in-Aid for R&D on orphan designated drugs (NIBN**)
Tax deduction for R&D expenses
Priority scientific consultation (PMDA)
Priority review (PMDA)
Premium at drug pricing
Extension of re-examination period***

***Market exclusivity period

PMDA
Making everyone's lives brighter together

Designated information

Name of drug

Name of applicant

Proposed indication or target disease

- ✓ Orphan drug designation is granted for the combination of drug, indication and applicant.
- ✓ Designated information is posted on the MHLW and NIBN website.
  https://www.mhlw.go.jp/stf/seisakunitsuite/bunya/0000068484.html
  List of designated drug: https://www.mhlw.go.jp/content/11120000/001261553.pdf
  https://www.nibn.go.jp/en/activities/orphan-support.html
  List of designated drug: https://www.nibn.go.jp/activities/promote/documents/hp_orphanlist_drug.pdf

PMDA
Making everyone's lives brighter together

Main players and roles related to orphan drug designation

MHLW

- Designation and approval of orphan drugs
- Designation consultation for orphan drugs
- Payment for the operational cost of NIBN
- Policy making related to designation and approval of orphan drugs
- Measures against intractable diseases, such as promotion of research and reduction of co-payment of medical fees

collaboration

PMDA

- Providing preliminary evaluation reports to assist MHLW's decision for orphan drug designation
- Priority scientific consultation during development stage
- Priority review of orphan drugs

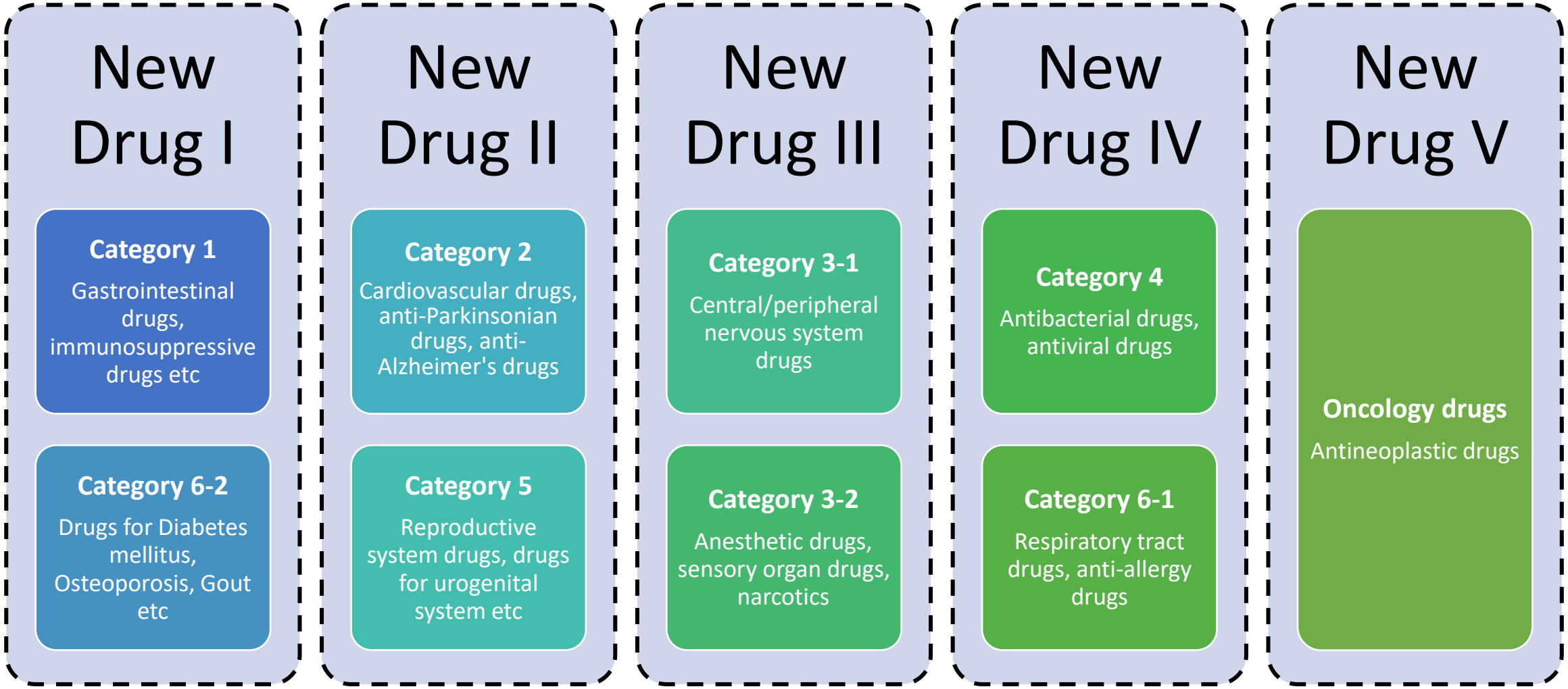
collaboration

NIBN

- Grant-in-Aid payment to the applicant
- Certification for research expenses for tax deduction
- Provision of guidance and consultation to the applicant

MHLW : Ministry of Health, Labour and Welfare
PMDA: Pharmaceuticals and Medical Devices Agency
NIBN : National Institutes of Biomedical Innovation, Health and Nutrition

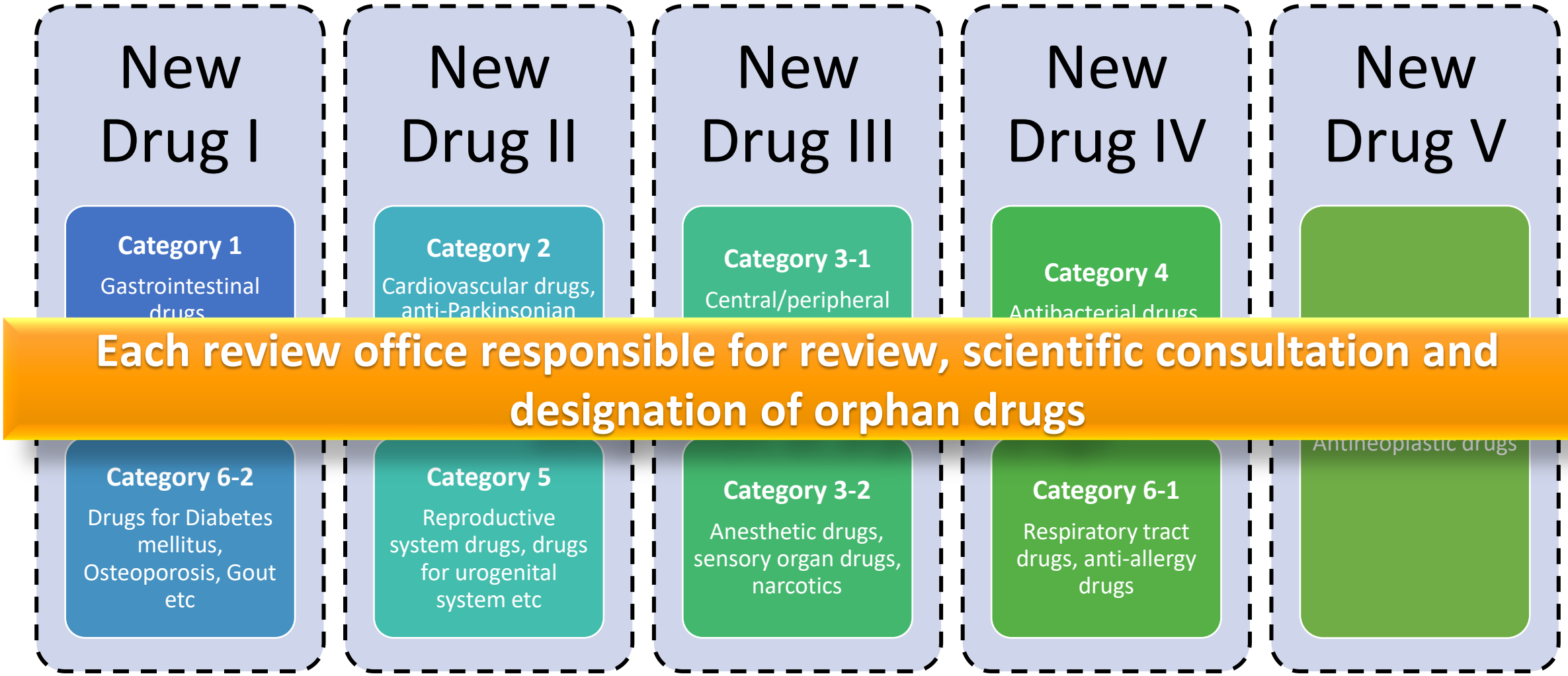
PMDA offices responsible for orphan drugs



[Others] Office of Cellular and Tissue-based Products, Office of Vaccines and Blood Products

PMDA
Making everyone's lives brighter together

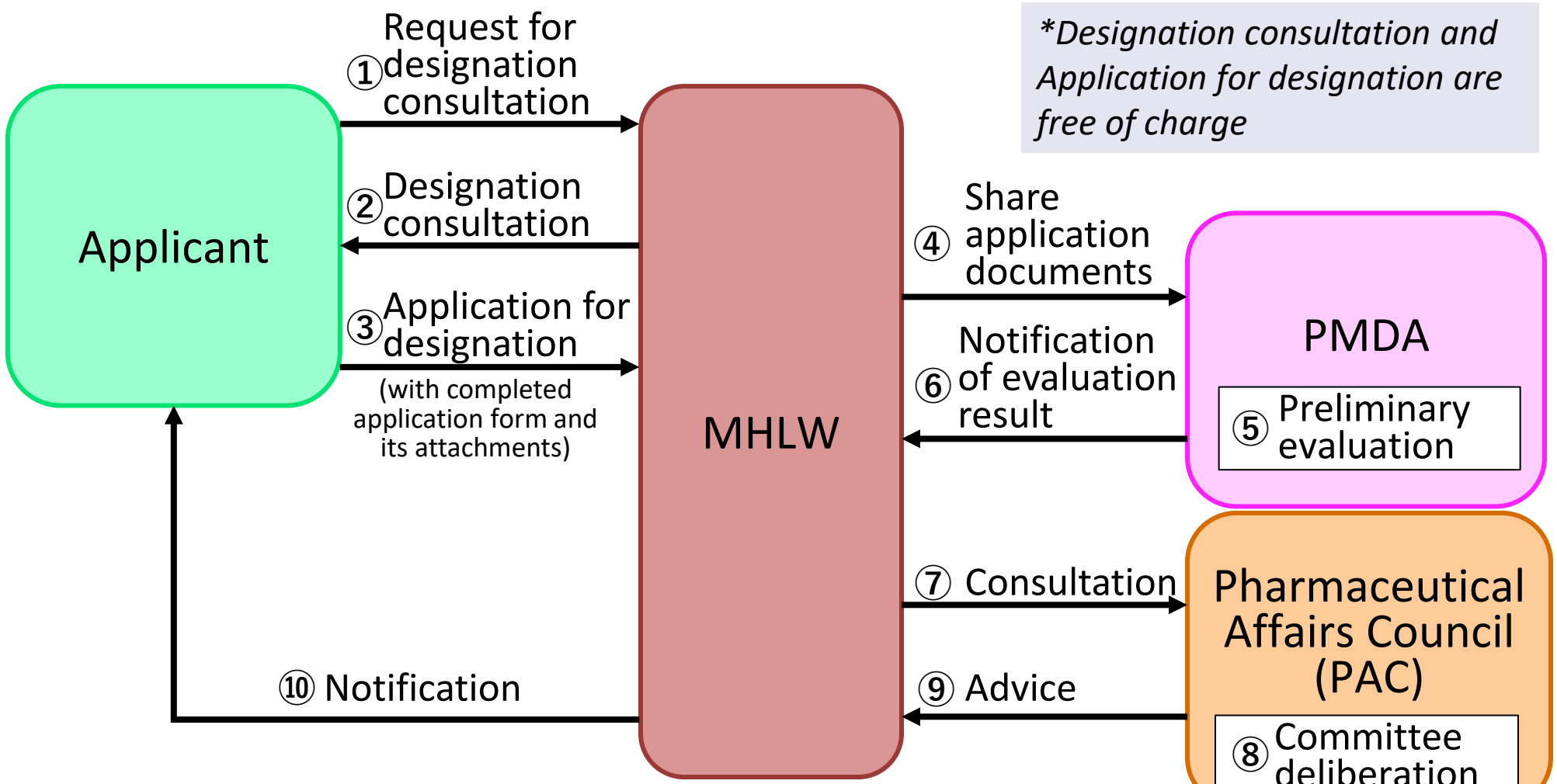
PMDA offices responsible for orphan drugs



[Others] Office of Cellular and Tissue-based Products, Office of Vaccines and Blood Products

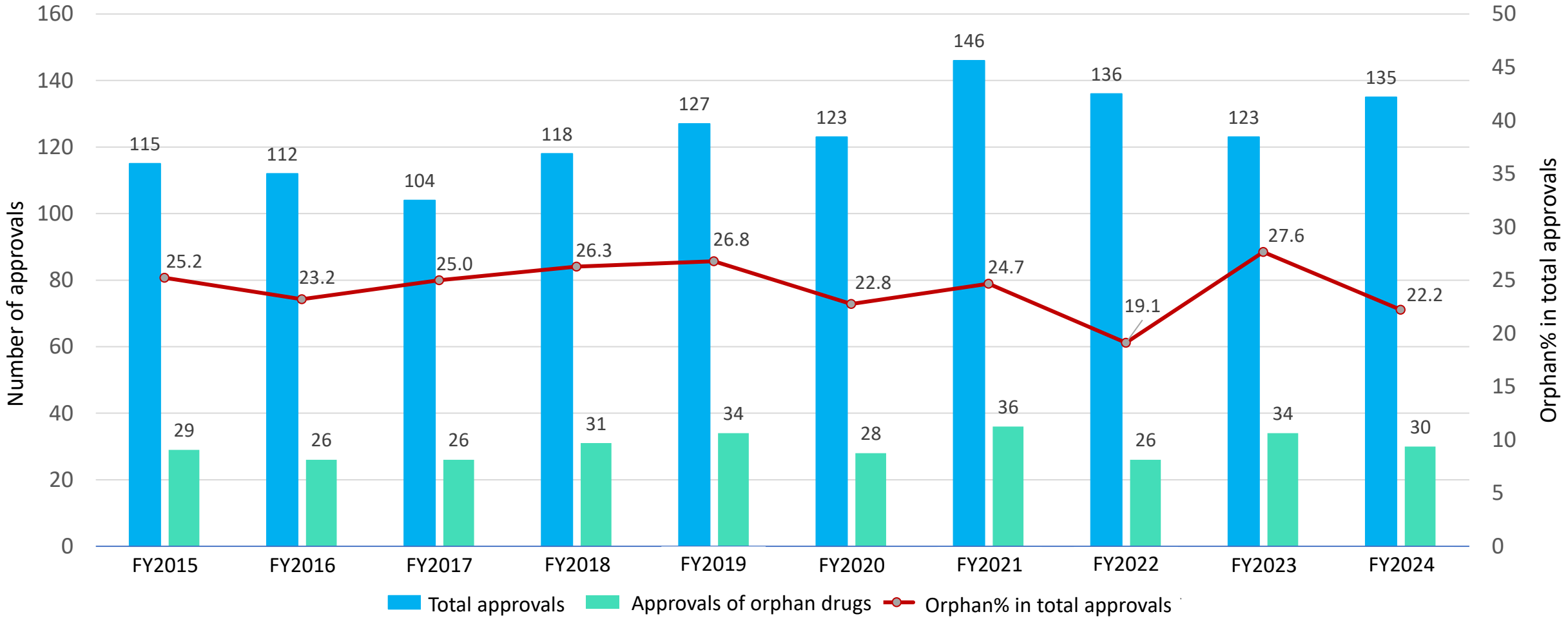
PMDA
Making everyone's lives brighter together

Flow for granting orphan drug designation



PMDA
Making everyone's lives brighter together

Recent trend in approvals in Japan



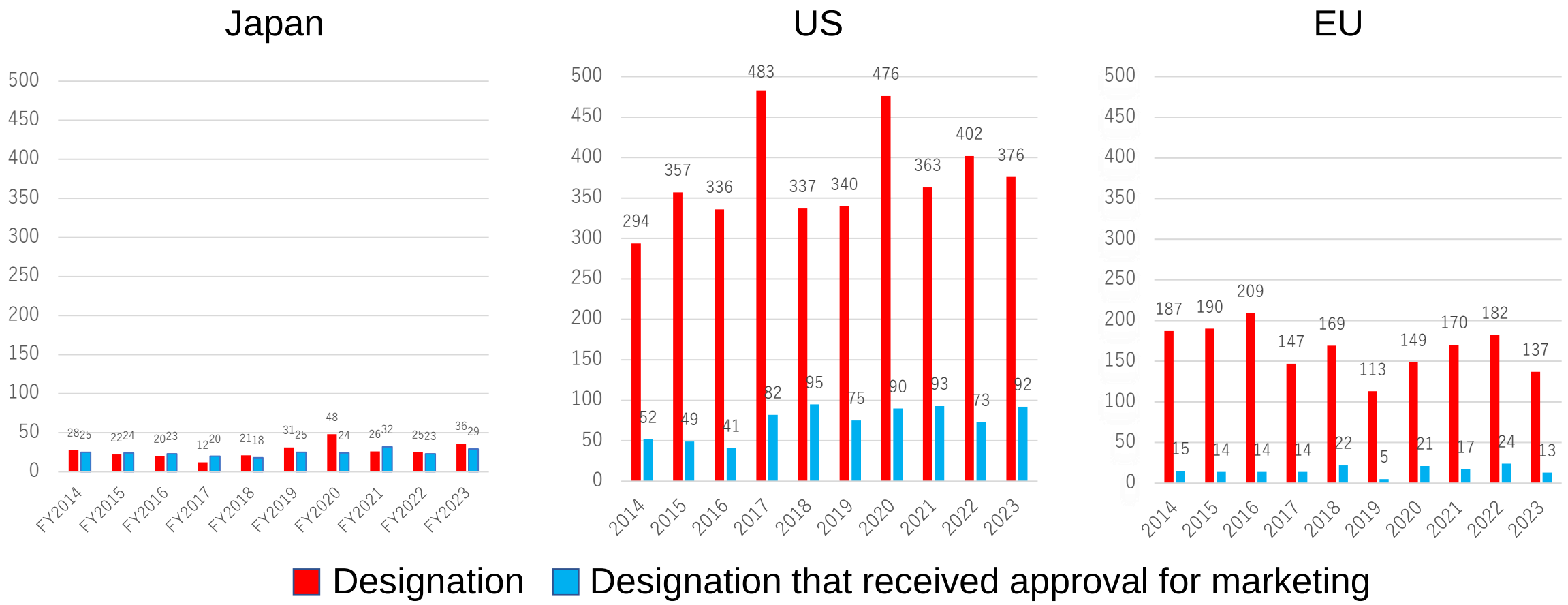
※ In addition to initial approvals, subsequent approvals for additional dosage forms etc were included in data aggregation.

PMDA
Making everyone's lives brighter together

- Orphan drug designation system in Japan
- **Recent regulatory efforts to further promote orphan drug development in Japan**

PMDA
Making everyone's lives brighter together

[Background] Trends in orphan drug designation and approval



※Source：https://www.accessdata.fda.gov/scripts/opdlisting/oopd/index.cfm（September 2025）
https://www.ema.europa.eu/en/human-regulatory/overview/orphan-designation-overview（September 2025）

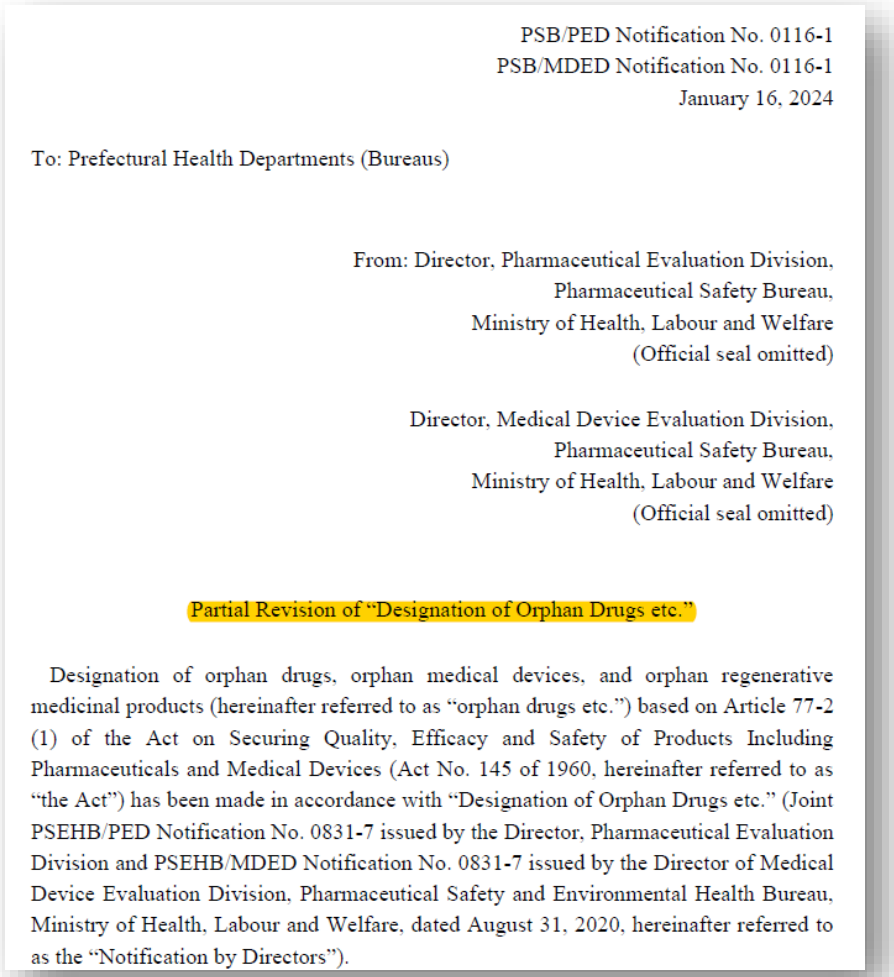
PMDA
Making everyone's lives brighter together

[Background] Comparison of designation criteria

Japan	US	EU
Meet **all** of the following • Patient population (less than 50,000 in Japan, or the target disease is one of the designated intractable disease) • Serious diseases with high medical needs • Possibility of development	Meet **any** of the following • Less than 200,000 patients in the United States • It is difficult to recoup development costs in the United States	Meet **all** of the following • Patient population (5 patients per 10,000 people) • Life-threatening or chronically debilitating disease • Medical needs

PMDA
Making everyone's lives brighter together

Revisions of orphan drug designation criteria in Japan



PSB/PED Notification No. 0116-1
PSB/MDED Notification No. 0116-1
January 16, 2024

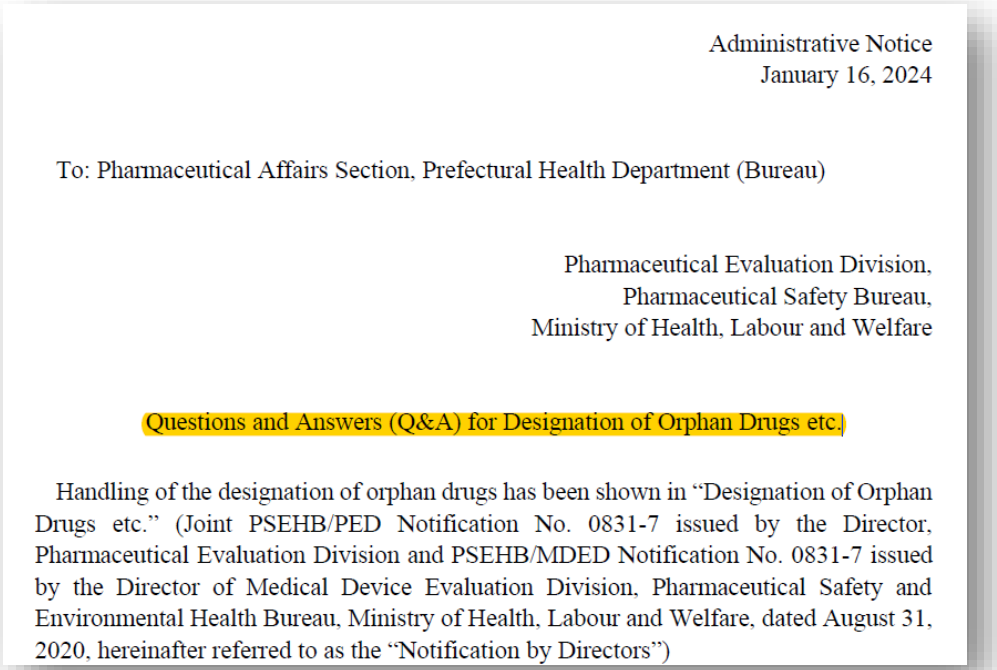
To: Prefectural Health Departments (Bureaus)

From: Director, Pharmaceutical Evaluation Division,
Pharmaceutical Safety Bureau,
Ministry of Health, Labour and Welfare
(Official seal omitted)

Director, Medical Device Evaluation Division,
Pharmaceutical Safety Bureau,
Ministry of Health, Labour and Welfare
(Official seal omitted)

Partial Revision of "Designation of Orphan Drugs etc."

Designation of orphan drugs, orphan medical devices, and orphan regenerative medicinal products (hereinafter referred to as "orphan drugs etc.") based on Article 77-2 (1) of the Act on Securing Quality, Efficacy and Safety of Products Including Pharmaceuticals and Medical Devices (Act No. 145 of 1960, hereinafter referred to as "the Act") has been made in accordance with "Designation of Orphan Drugs etc." (Joint PSEHB/PED Notification No. 0831-7 issued by the Director, Pharmaceutical Evaluation Division and PSEHB/MDED Notification No. 0831-7 issued by the Director of Medical Device Evaluation Division, Pharmaceutical Safety and Environmental Health Bureau, Ministry of Health, Labour and Welfare, dated August 31, 2020, hereinafter referred to as the "Notification by Directors").



Administrative Notice
January 16, 2024

To: Pharmaceutical Affairs Section, Prefectural Health Department (Bureau)

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

Questions and Answers (Q&A) for Designation of Orphan Drugs etc.

Handling of the designation of orphan drugs has been shown in "Designation of Orphan Drugs etc." (Joint PSEHB/PED Notification No. 0831-7 issued by the Director, Pharmaceutical Evaluation Division and PSEHB/MDED Notification No. 0831-7 issued by the Director of Medical Device Evaluation Division, Pharmaceutical Safety and Environmental Health Bureau, Ministry of Health, Labour and Welfare, dated August 31, 2020, hereinafter referred to as the "Notification by Directors")

The notification and Q&A document were issued in January 2024.
https://www.pmda.go.jp/english/review-services/regulatory-info/0012.html#orphan_drugs

PMDA
Making everyone's lives brighter together

Revisions of orphan drug designation criteria in Japan

	Old	New
Number of subjects	● The number of subjects pertaining to the usage of the drugs is less than 50,000 in Japan. (In principle, so-called "salamislicing"(=orphan subset without any clear medical or pharmaceutical reasons) is NOT acceptable.) ● For a designated intractable disease, less than the number of subjects specified in the Designated Intractable Disease Act	➔Expanded the range of orphan subset considered acceptable
Medical needs	● For serious diseases ● High medical needs that meet either of the following: ✓ No appropriate alternative drugs etc. or treatments ✓ Expected to have significantly higher efficacy and safety compared to existing drugs etc.	➔Clarified and added some examples
Possibility of development	● There are rationales for the use of the drugs for the target disease ● Its development plan is recognized to be appropriate	➔Clarified

PMDA
Making everyone's lives brighter together

1. Number of subjects

- The number of subjects pertaining to the usage of the drugs is less than 50,000 in Japan
  - ➢ In principle, so-called “salami slicing” (=orphan subset without any clear medical or pharmaceutical reasons) is NOT acceptable.
  - ➢ Orphan subset for which advancement in drug development is limited despite high unmet needs is considered acceptable if the subset is based on appropriate medical and pharmaceutical evidence including the age range (including pediatrics), treatment algorithm and line, risk classification, and the necessity of medication etc..

New!

- For a designated intractable disease, less than the number of subjects specified in the Designated Intractable Disease Act

2. Medical needs

- For serious diseases
- For drugs that meet any of the following to support clinical benefit for the target disease
  - No approved drugs
  - Approved drugs exist, but the prognosis of the target disease is poor even treated with those drugs. Therefore multiple options are clinically needed.
  - Drugs expected to be more effective and safer compared to approved drugs

Clarified!

For example,

Added!

(1) based on the head-to-head comparison in an appropriately designed clinical study
(2) based on the indirect comparison of multiple clinical studies etc.
(3) Prioritized over the approved drug in major guidelines based on a scientific evidence
(4) High probability of being superior in safety because the safety profile is completely different

PMDA
Making everyone's lives brighter together

3. Possibility of development

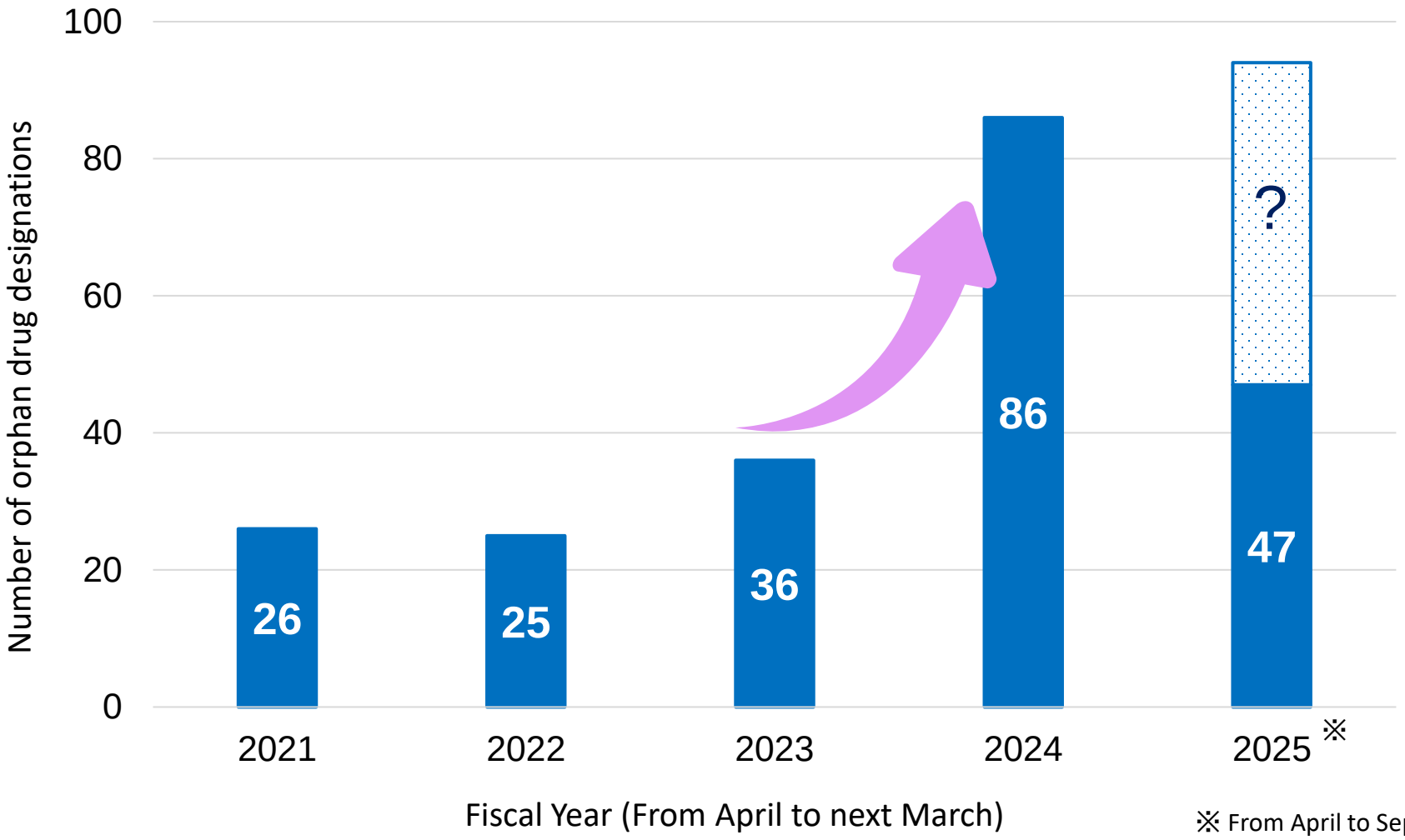
- Its development plan is recognized to be appropriate

- Having organizations and plans that enable development in Japan.

With this revisions of orphan drug designation criteria, MHLW/PMDA expect that the possibilities of developing orphan drugs including Japan will be increased.

PMDA
Making everyone's lives brighter together

Recent trends in orphan drug designation in Japan



※ From April to September

PMDA
Making everyone's lives brighter together

Gate Opening Summit for Innovative Drug Discovery

July 30, 2024

Prime Minister Kishida delivering an address (1)

https://japan.kantei.go.jp/101_kishida/actions/202407/30souyaku.html

Strategic Goal and Action Plan

for Improving Drug Discovery Capabilities to Support Early Availability of Innovative Drug

Number designated as orphan drugs

151 (cumulative from FY2018 to FY2022)

↓

200 (cumulative from FY2024 to FY2028)

PMDA

Making everyone’s lives brighter together