16th DIA Japan Annual Meeting 2019

- Delivering Rational Medicine for All People in the Globe -

November 10-12, 2019 | Tokyo Big Sight

Current situation and future perspectives of review and scientific consultation about orphan drugs

Yoko Aoi, PhD
Principal Reviewer
Office of New Drug V, PMDA Japan

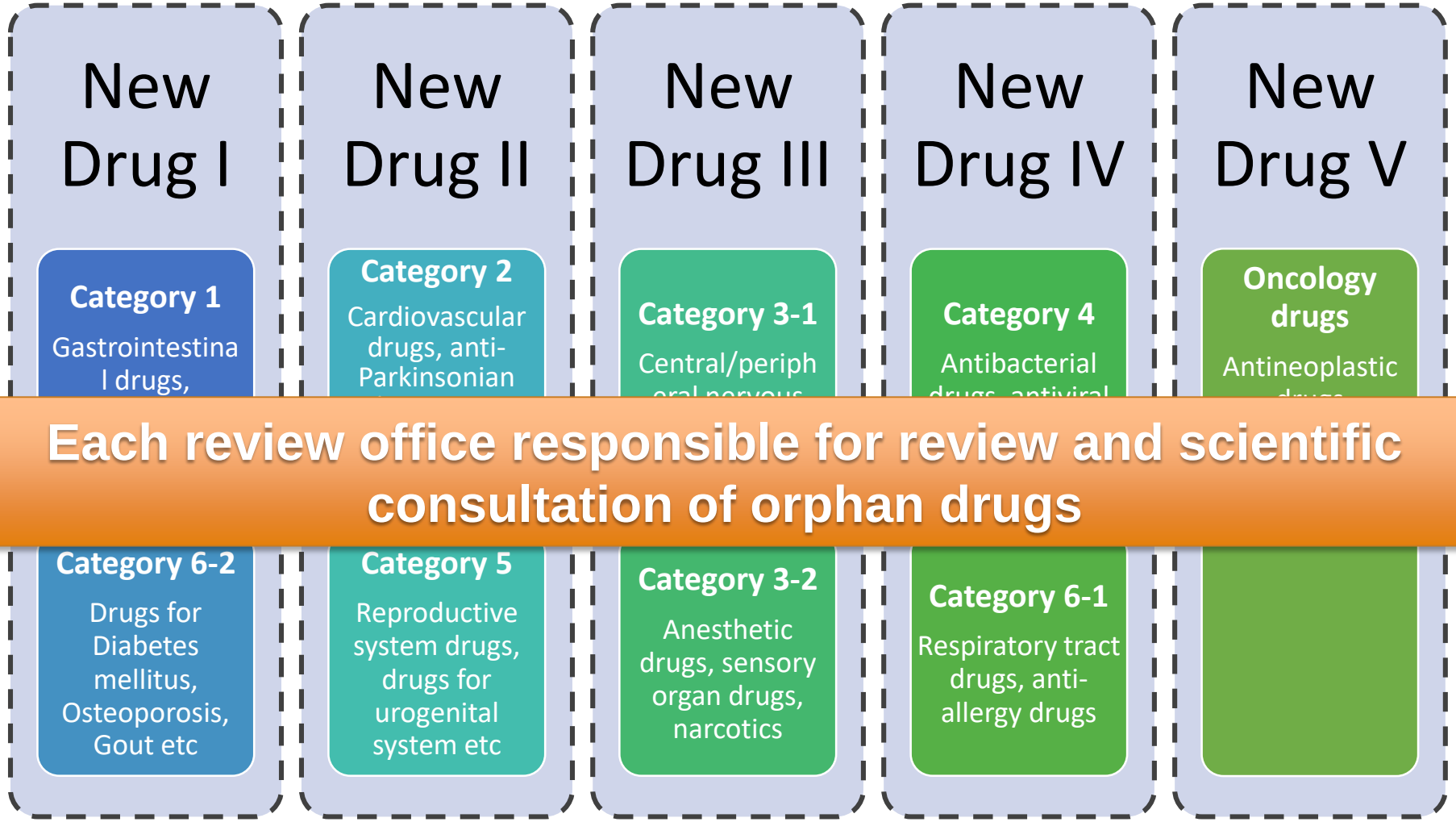
DIA

Disclaimer

- The views and opinions expressed in the following PowerPoint slides are those of the individual presenter and should not be attributed to DIA, its directors, officers, employees, volunteers, members, chapters, councils, Communities or affiliates, or any organization with which the presenter is employed or affiliated.
- These PowerPoint slides are the intellectual property of the individual presenter and are protected under the copyright laws of the United States of America and other countries. Used by permission. All rights reserved. DIA and the DIA logo are registered trademarks or trademarks of Drug Information Association Inc. All other trademarks are the property of their respective owners.

System and framework for promoting orphan drug development

PMDA framework for orphan drugs



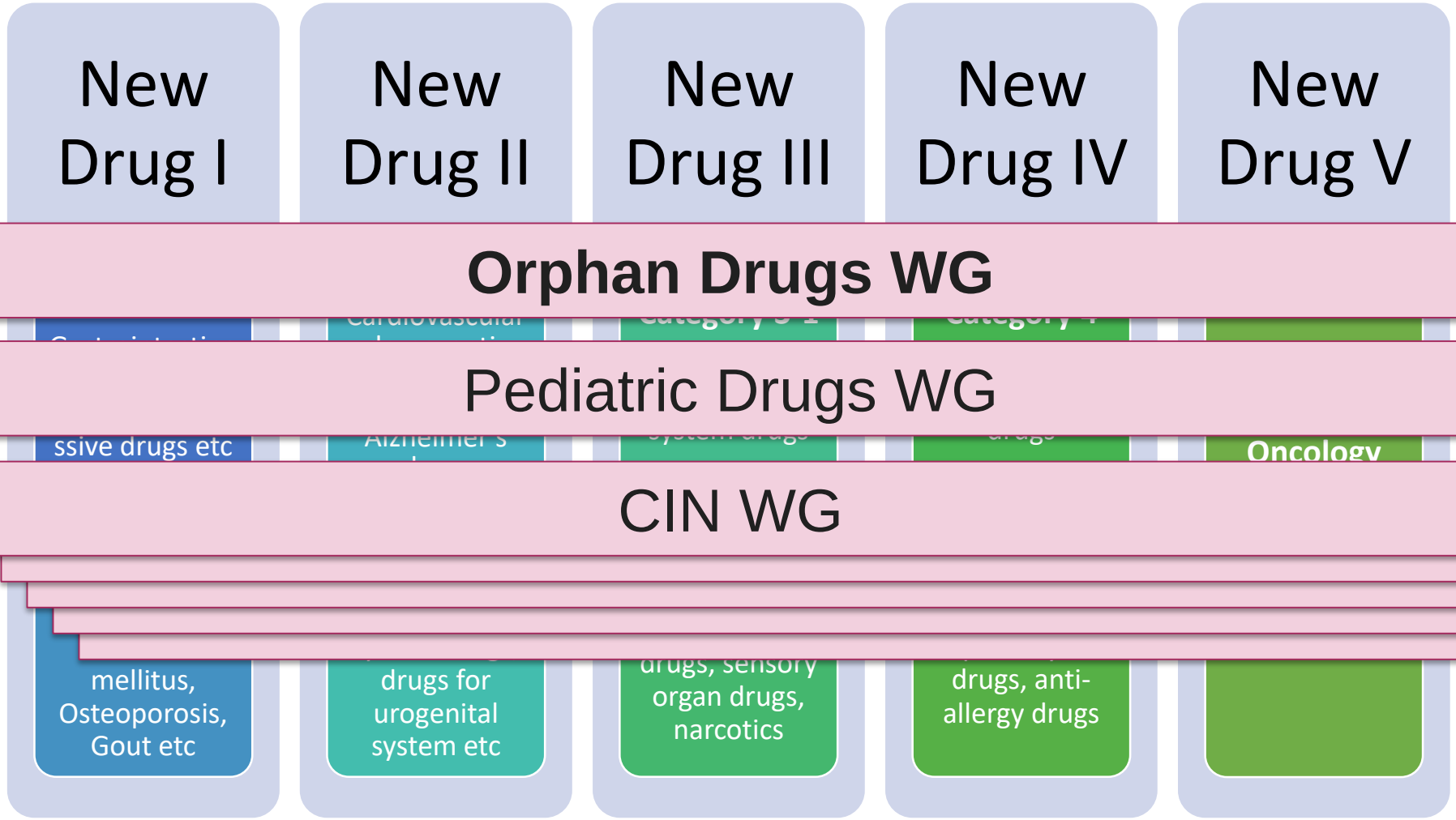
[Others] Office of Cellular and Tissue-based Products, Office of Vaccines and Blood Products

Projects across Multi-Offices in PMDA

- Cardiovascular Risk Evaluation WG
- Clinical Innovation Network WG
- Companion Diagnostics WG
- Global Clinical Study WG
- ICH Q12 WG
- iPSC (Induced pluripotent stem cells) WG
- Innovative Manufacturing Technology WG
- Nanomedicine Initiative WG
- Omix WG
- **Orphan Drugs WG**
- Patient Centricity WG
- Pediatric Drugs WG

Who are involved in Projects across Multi-Offices

PMDA framework for orphan drugs



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

Orphan Drugs Working Group in PMDA

Objectives

To make proposals for supportive measures for facilitating the orphan drug development

Activities

- **Perceive issues and new movements pertaining to orphan drug development**
  - Analyze previous experience regarding orphan drug development and review
  - Collect information regarding new approaches for orphan drug development driven by advancement of science
- **Strengthen collaboration with other regulatory agencies for orphan drug development**
  - Terms of reference between PMDA and EMA (2012)

Orphan drugs – Designation system

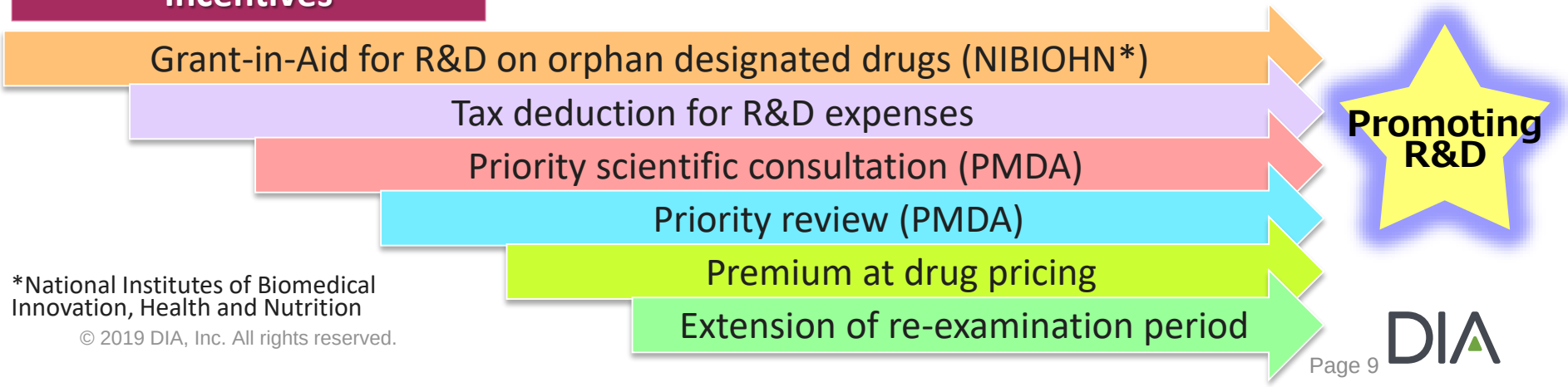
Aim

✓ 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 patients
   - Less than 50,000 in Japan
   - The target disease is one of the designated intractable disease
2. Medical needs
   - For serious diseases with high medical needs
3. Feasibility of development

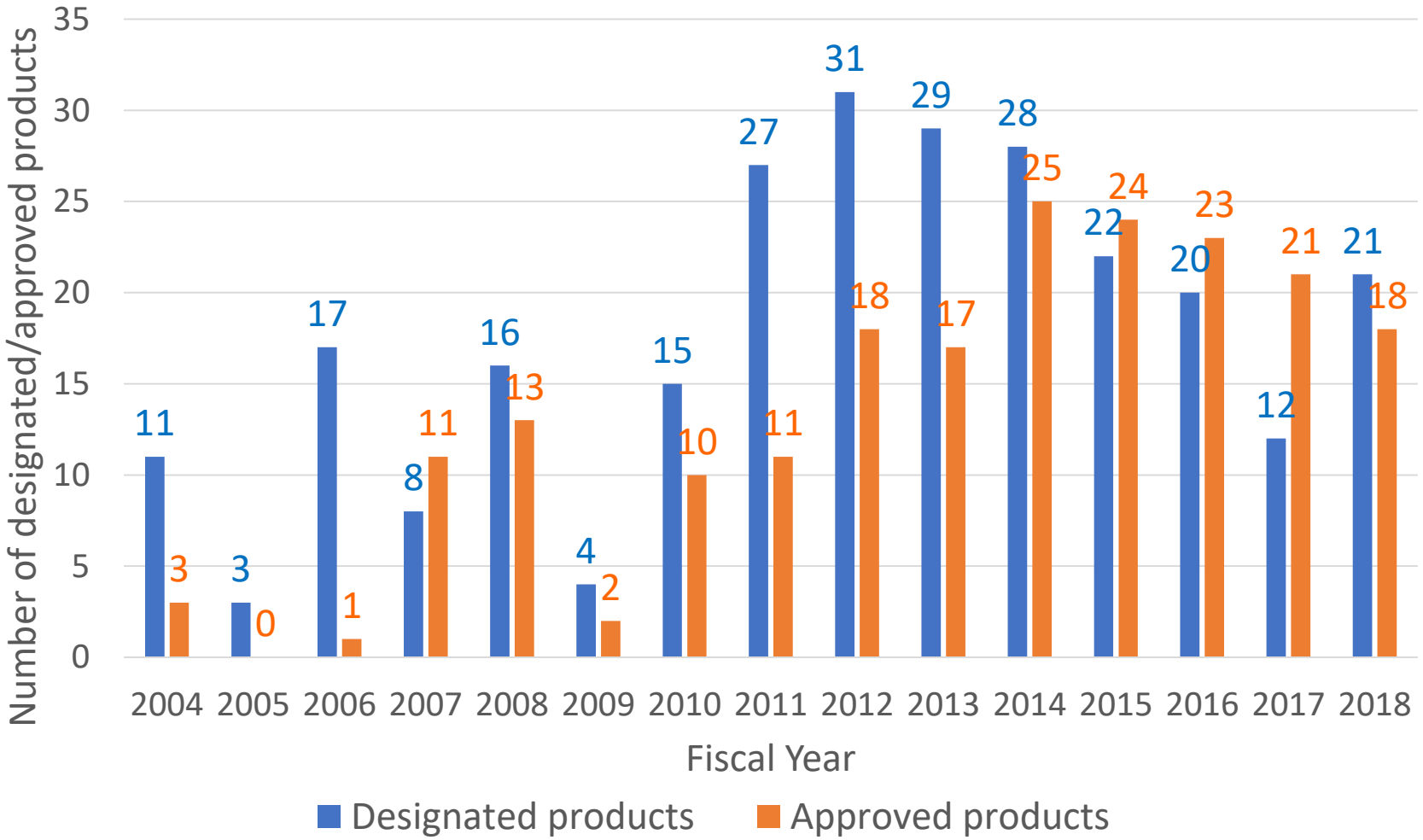
Incentives



*National Institutes of Biomedical Innovation, Health and Nutrition

Current situation on orphan drug development
- How to cope with various difficulties? -

Trend in designation and approval of orphan drugs in Japan



Designated products (264 in total) is counted based on designation from FY2004 to 2018.
Approved products (197 in total) is counted based on approval from FY2004 to 2018.

Difficulties when planning/designing and conducting clinical trials of orphan drugs

- Disease is not well-defined
- Subject recruitment doesn't proceed as expected
- Endpoints are not well-established
- Randomized controlled trial (RCT) is possible in some cases, but there could be more obstacles to set a control group.

  When planning open-label, single arm trials,
  - how to explain natural history without the investigational drug?
  - how to set criteria for success of the trial?

Past experiences to deal with these difficulties

- Immature disease definition
- Unestablished endpoints

  ⇨**Conduct comprehensive literature review**

  ⇨**Hear opinions from key opinion leaders**
- Difficult subject recruitment

  ⇨**Ask for cooperation of key opinion leaders**
- When planning open-label, single arm trials,
  - how to explain natural history without the investigational drug?
  - how to set criteria for success of the trial?

  ⇨**Refer to study results (e.g., foreign RCTs)**

  ⇨**Conduct comprehensive literature review**

Utilization of registries for development of drugs and medical devices

- ✓ Marketing research
- ✓ Survey for the feasibility of a clinical trial
- ✓ Subject recruitment for clinical trials
- ✓ Development of study protocol

e.g., for disease area where conduct of conventional clinical trials is difficult

- ✓ Utilization as an external control in clinical trials
  - ➢ Application dossier for marketing authorization
- ✓ Utilization for Post-Marketing Surveillance (PMS) and risk management
  - ➢ Application dossier for reexamination

To deal with increase in development cost and unmet medical needs

Further utilization of registries for development of drugs and medical devices and collection of post-marketing information are highly expected

DIA

Current and future perspectives to overcome these difficulties – 1

- Immature disease definition
- Unestablished endpoints
  - ⇨**Conduct comprehensive literature review**
  - ⇨**Hear opinions from key opinion leaders**
  - ⇨**Disease/Patient registries could contribute to establishment of disease concept, disease definition and endpoint.**
- Difficult subject recruitment
  - ⇨**Ask for cooperation of key opinion leaders**
  - ⇨**Utilize registries as a platform to find out potential/eligible subjects**

Current and future perspectives to overcome these difficulties – 2

- When planning open-label, single arm trials,
  - how to explain natural history without the investigational drug?
  - how to set criteria for success of the trial?

⇨**Refer to study results (e.g., foreign RCTs)**

⇨**Conduct comprehensive literature review**

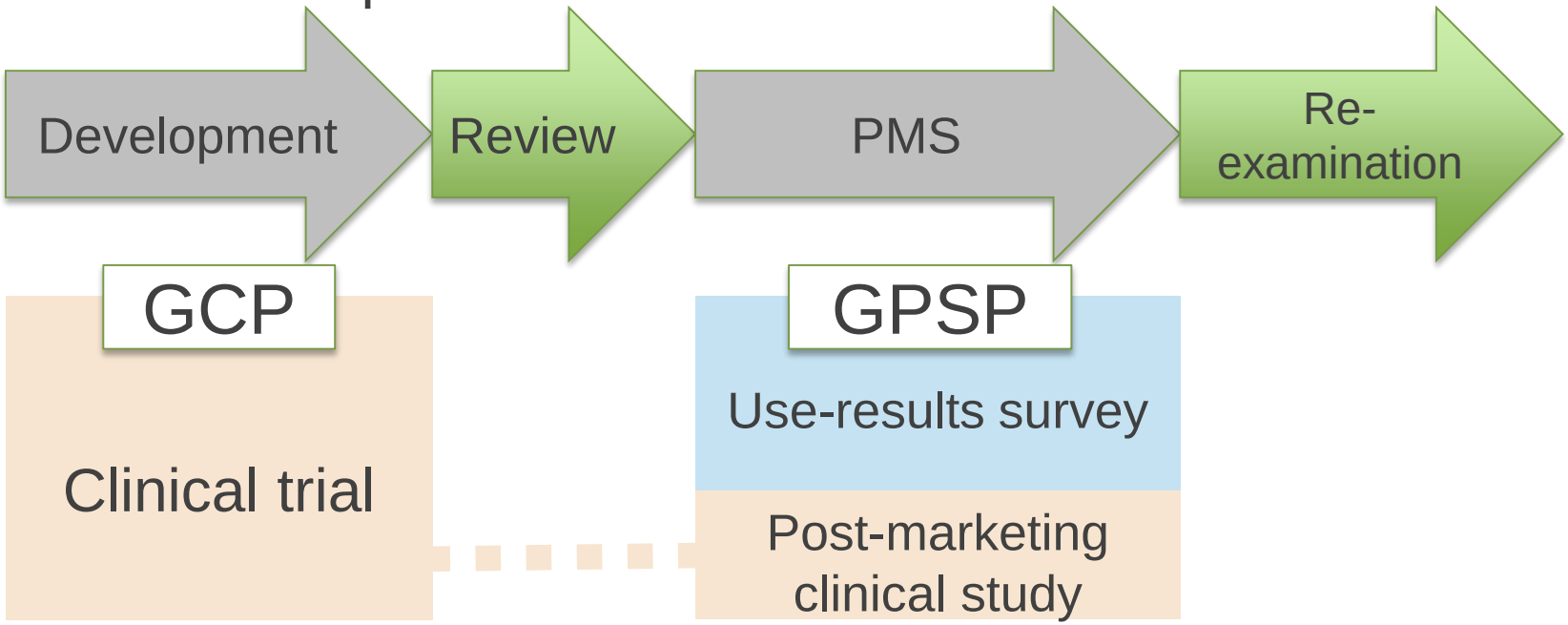
⇨**Possibility to utilize registries as external control?**

Discussion is ongoing among CIN WG

Applying Real-World Data (RWD) to orphan drugs

- Utilizing disease registry data

  From development to re-examination



e.g. Clinical trials for rare disease which is difficult to conduct RCTs

e.g. Conducting survey or study in a more efficient manner

PMDA's efforts toward utilization of RWD

1. New Consultation Category for Registry Utilization (piloted in FY2019)

- Multiple consultation categories for registry holders and product developers

  <u>For registry holders</u>

  ✓ General considerations to ensuring reliability of registry data for regulatory approval

  <u>For product developers</u>

  ✓ Advice on the development plan using registry and the reliability of the registry data for individual product

PMDA's efforts toward utilization of RWD

2. Preparation of Guideline for Product Development utilizing RWD

- Notification issued
  - Amended GPSP Ordinance
  - Basic Principle for Utilization of Medical Information Database in Post-Marketing Pharmacovigilance (2017.6.9)
  - Points to Consider for Ensuring the Data Reliability on Post-Marketing Database Study for Drugs (2018.2.21)
  - Points to Consider for Ensuring the Data reliability on Post-Marketing Database Study for Medical Devices (2018.12.19)
- **Basic principle for utilization of registry data for regulatory submission and points to consider for ensuring the data reliability are being developed**, considering experience from consultations and global circumstance.
  - **Drafts will be developed in FY2019**, and their finalization and publication is planned in FY2020 after discussion with experts.

DIA