

Japan's Regulatory Framework and Recent Updates on Regenerative Medical Products

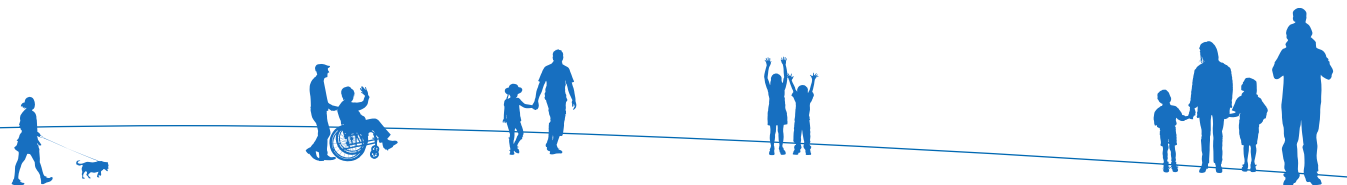
KISHIOKA Yasuhiro, Ph.D.

Review Director

Office of Cellular and Tissue-based Products

Pharmaceuticals and Medical Devices Agency (PMDA)

The views and opinions expressed in this presentation are those of the presenter and should not necessarily represent the views and opinions of the PMDA.



Outline

- Introduction
 - Japanese Regulatory authorities (MHLW and PMDA)
 - PMDA and its Organizational Structure
 - Review Process of MAA for RMPs
- Regulatory History and Current Status of RMPs
 - Safety Act and PMD. Act
 - RMPs approved in Japan
 - Number of Clinical Trial Notifications/Consultations
 - Orphan Designation, SAKIGAKE Designation, and Conditional and Time-limited Approval
- Collaboration with international regulators and Outreach Initiatives

MHLW: Ministry of Health Labour and Welfare
MAA: Marketing Authorization Application
RMPs: Regenerative Medical Products
PMD. Act: the Act on Pharmaceuticals and Medical Devices



Regulatory Authorities in JAPAN

MHLW

Ministry of Health Labour and Welfare

- Final authorization of applications
- Publishing Guidelines
- Advisory committee
- Supervising PMDA Activities

PMDA

- Scientific Review for Drugs, Medical Devices and Regenerative Medical Products
- GCP, GMP/GCTP Inspection
- Consultation for development
- Safety Measures
- Relief Services



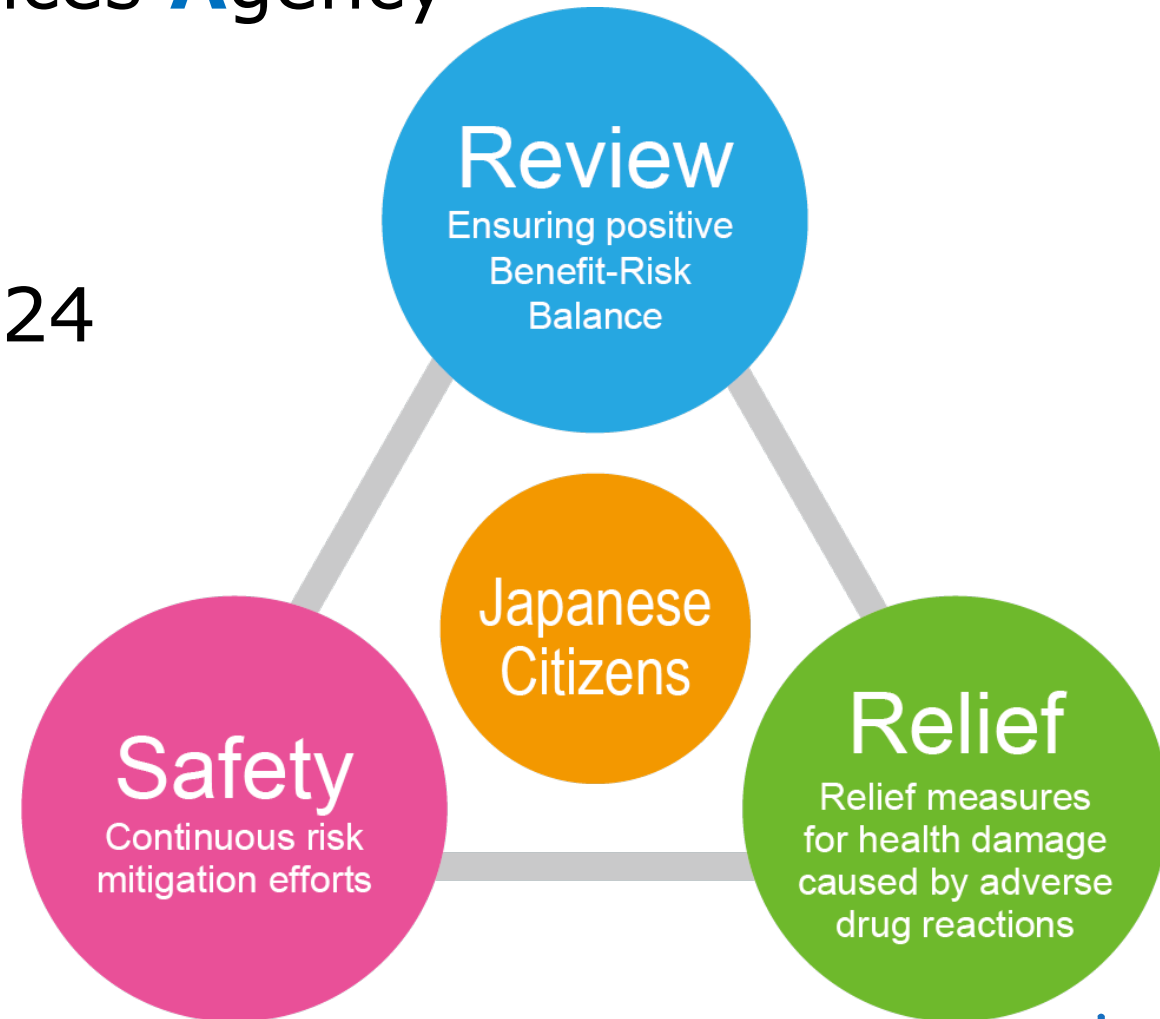
独立行政法人 医薬品医療機器総合機構
Pharmaceuticals and Medical Devices Agency



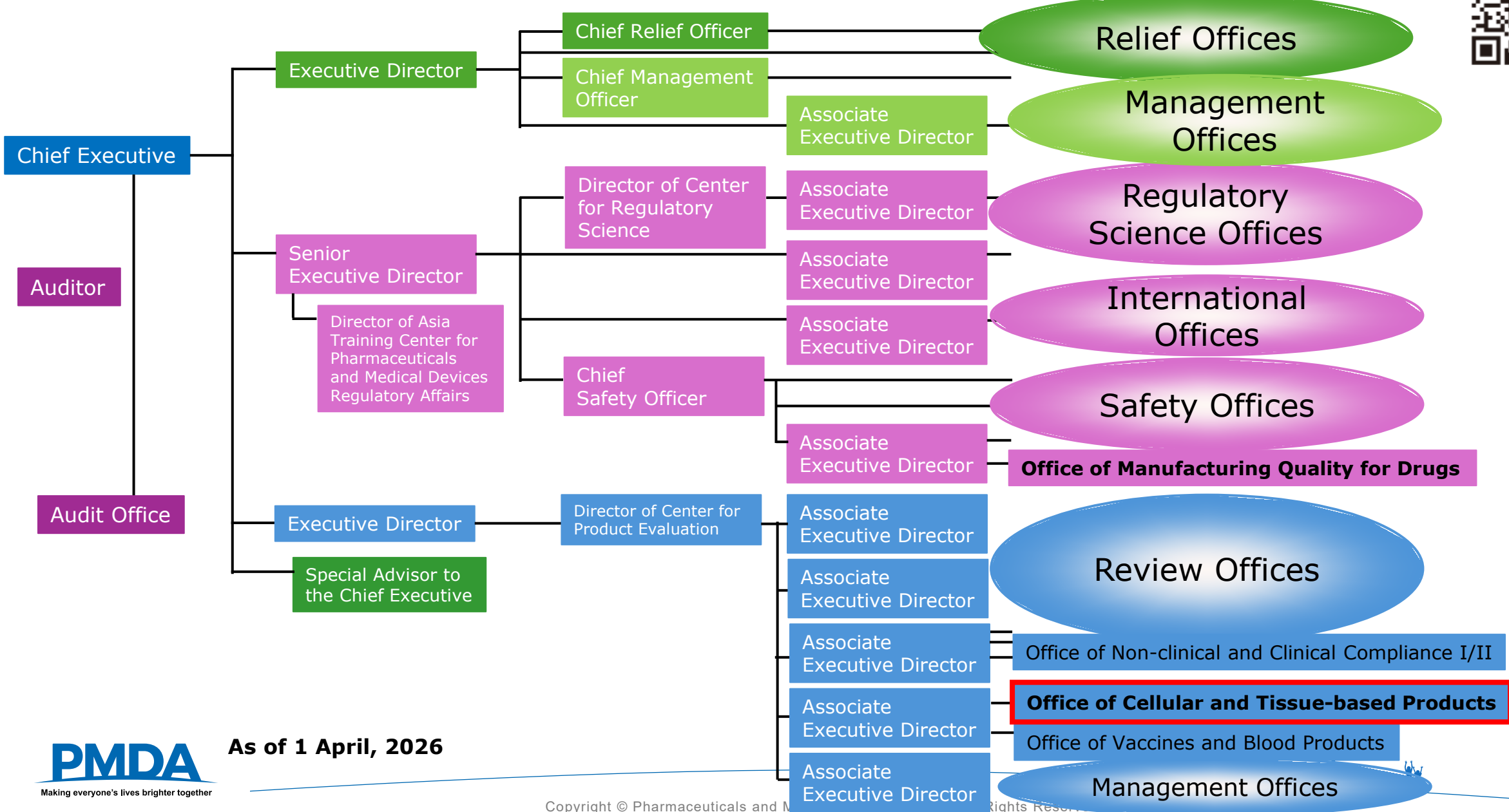
PMDA

Pharmaceuticals and Medical Devices Agency

- Established on 1 April, 2004
- 1,063 Employees, as on April 2024
 - Review Department; 635
 - Safety Department; 261
 - Relief Department; 41



Organizational Structure of PMDA

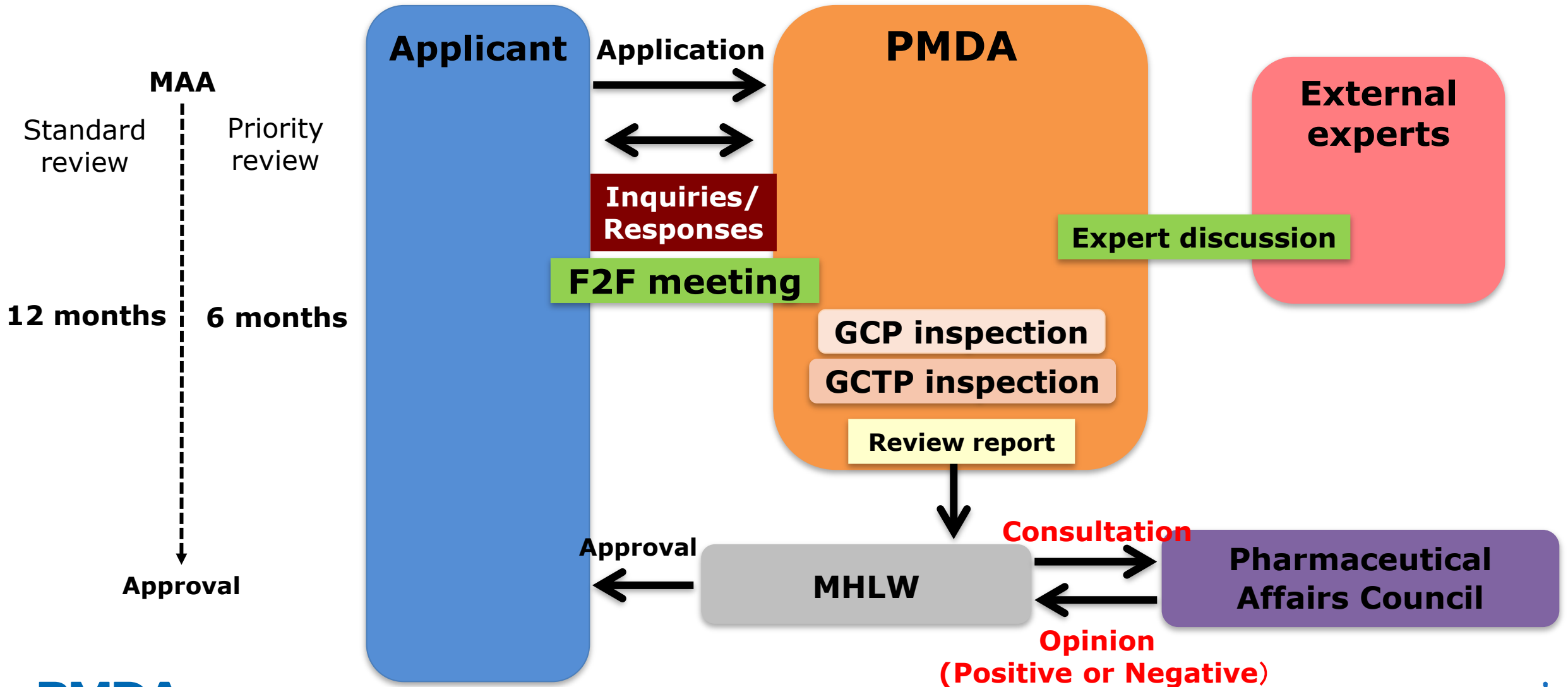


As of 1 April, 2026



Review Process of MAA for RMPs in Japan

MAA: Marketing Authorization Application



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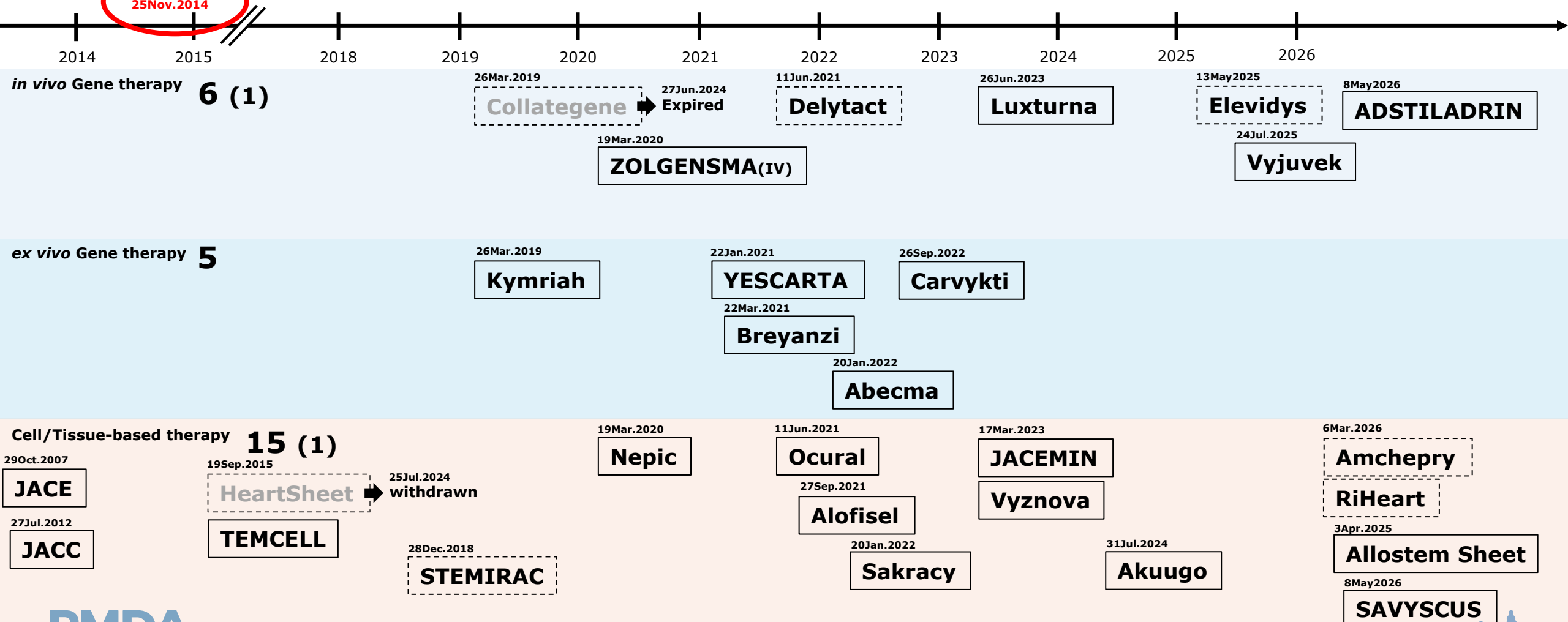
Regulatory History and Status of RMPs

As of 20 May, 2026

“Regenerative Medical Products” (RMPs) has been defined under the Act on Pharmaceuticals and Medical Devices (PMD. Act)

25Nov.2014

continuously published/updated relevant guidelines



Regulatory Reform in 2014



Safety
Act

The Act on the Safety of Regenerative Medicine



PMD
Act

Revision of the Pharmaceutical Affairs Law:
The Act on Pharmaceuticals and Medical Devices

Enacted on 25 November 2014

2014

These two acts were promulgated in November 2013 by the Japanese Diet (Parliament) in line with the **Regenerative Medicine Promotion Act** in order to reform the pharmaceutical and medical regulation related to regenerative medicine.

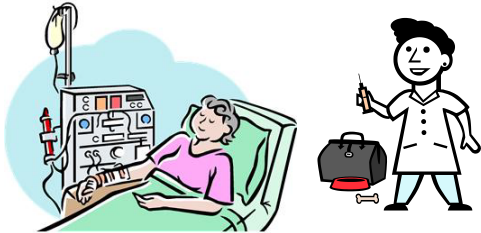


Two Acts Regulating Regenerative Medicine in Japan

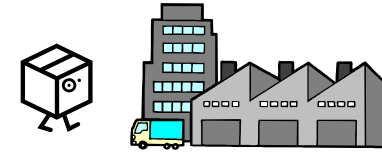
Technology & Product

Regenerative Medicine

All medical **technologies** using processed cells which safety and efficacy have not yet been established



Production and marketing of regenerative and cellular therapeutic **products** by firms



Safety Act

The Act on the Safety of Regenerative Medicine

Medical Care or Academic Research Purpose

The Act on Pharmaceuticals and Medical Devices

PMD Act

Commercial Product Marketing Authorization Purpose



RMPs; Definition under PMD. Act

Article 2-(9)-(i),(ii):

The term "regenerative medicine product" used in this Act refers to the following items (excluding quasi-pharmaceutical products and cosmetics), as specified by Cabinet Order:

- (i) the following items intended for use in human or animal healthcare which are obtained after culturing or other processes using human or animal cells:
 - (a) reconstruction, repairing or formation of the structure or function of the bodies of humans or animals;
 - (b) treatment or prevention of disease in humans or animals;
- (ii) items intended for use in the treatment of disease in humans or animals which are introduced into cells of humans or animals and contain genes to be expressed in their bodies.

- Cellular and tissue-based products

e.g.,

- CAR-T cell products
- Cultured cartilage

- Gene therapy products

e.g.,

- Recombinant viral vector products
- mRNA products except vaccines



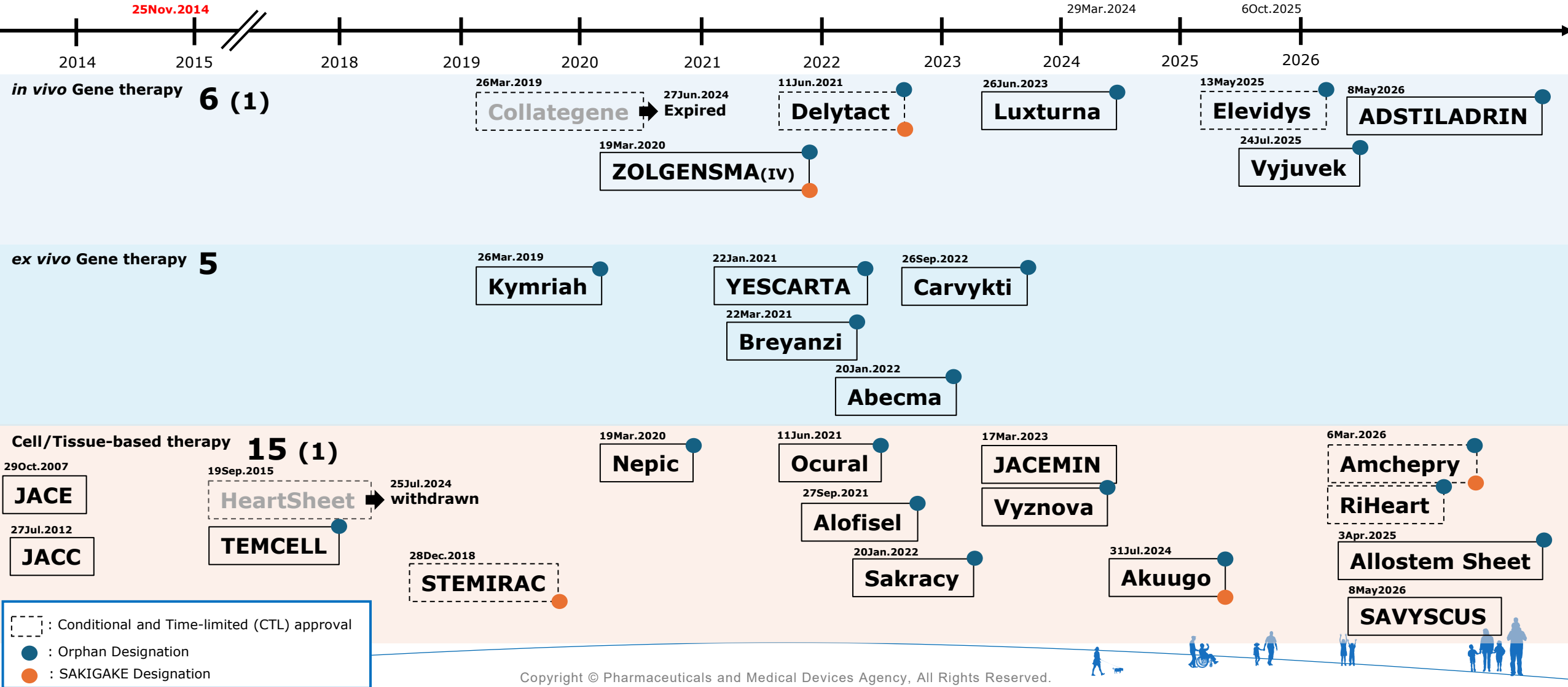
Regulatory History and Status of RMPs

As of 20 May, 2026

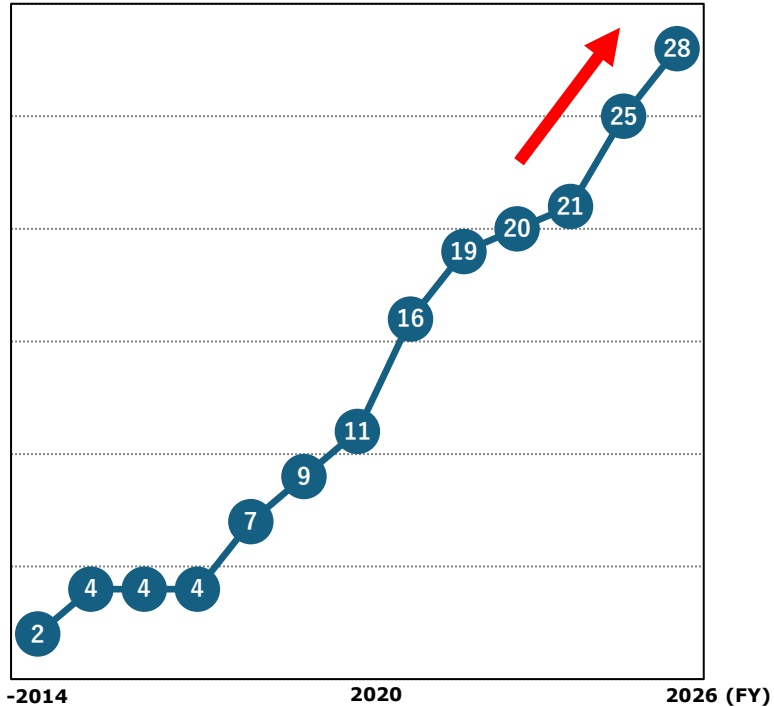
“Regenerative Medical Products” (RMPs) has been defined under the Act on Pharmaceuticals and Medical Devices (PMD. Act)



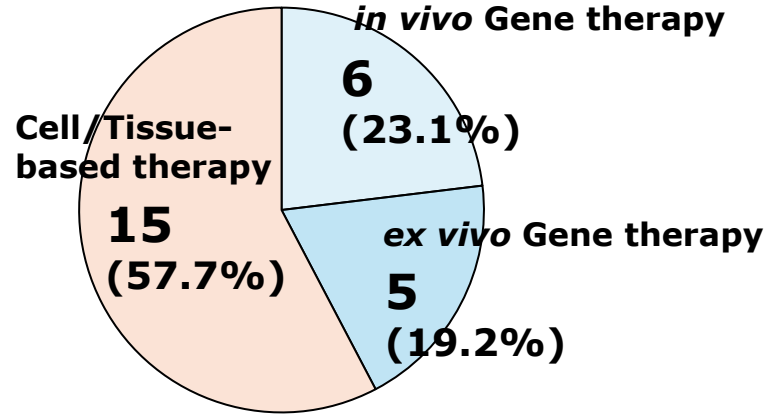
continuously published/updated relevant guidelines



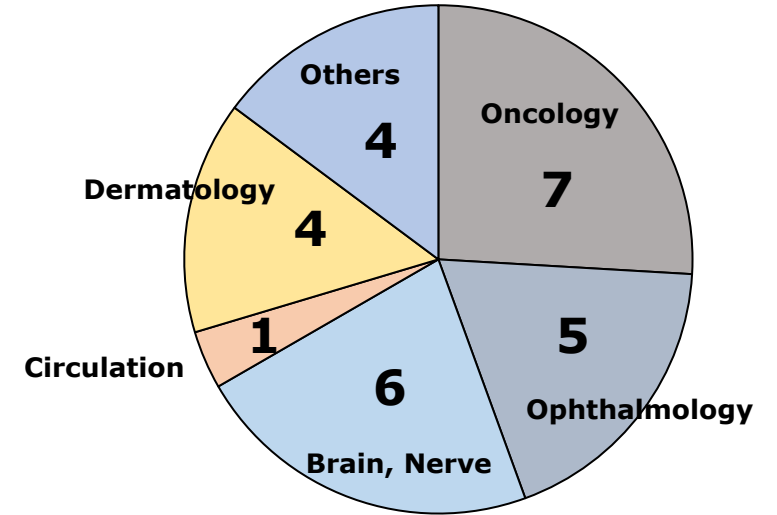
Approved RMPs in Japan: Key Statistics and Trends



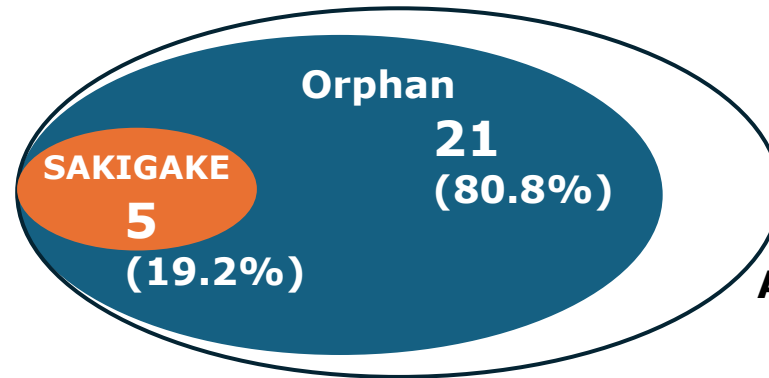
No. of approved RMPs (Fig.1)



Type (Fig.2)



Area of disease (Fig.4)



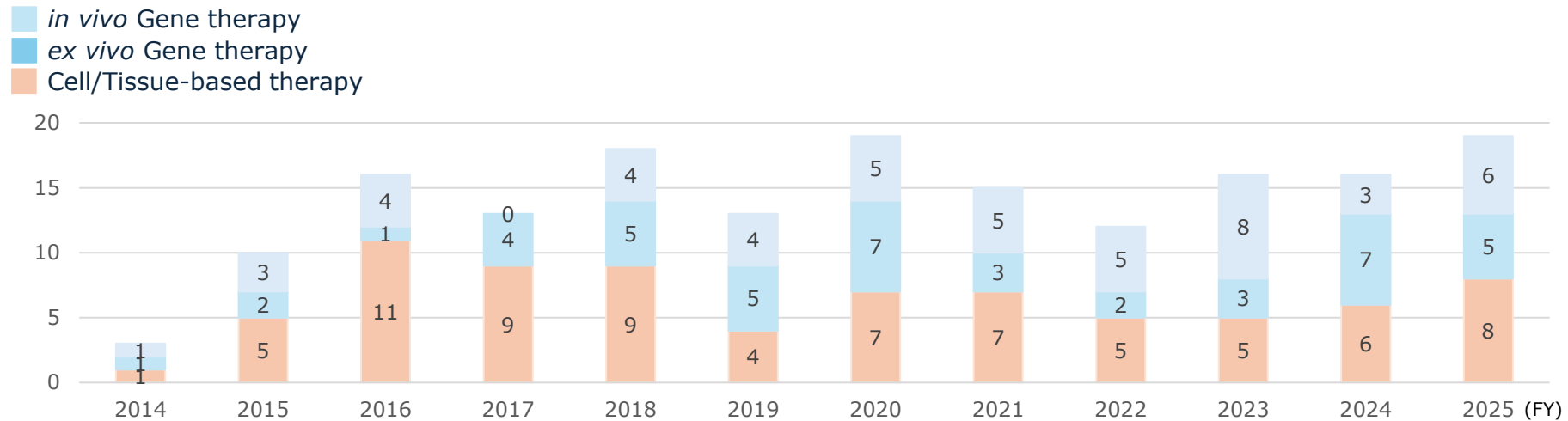
Designation (Fig.3)

Fig.1: Approval includes two products that were withdrawn or expired. Figs.2-4: Excludes two withdrawn or expired approvals
Figs.3 and 4: Based on the originally approved indication; indication extensions not considered

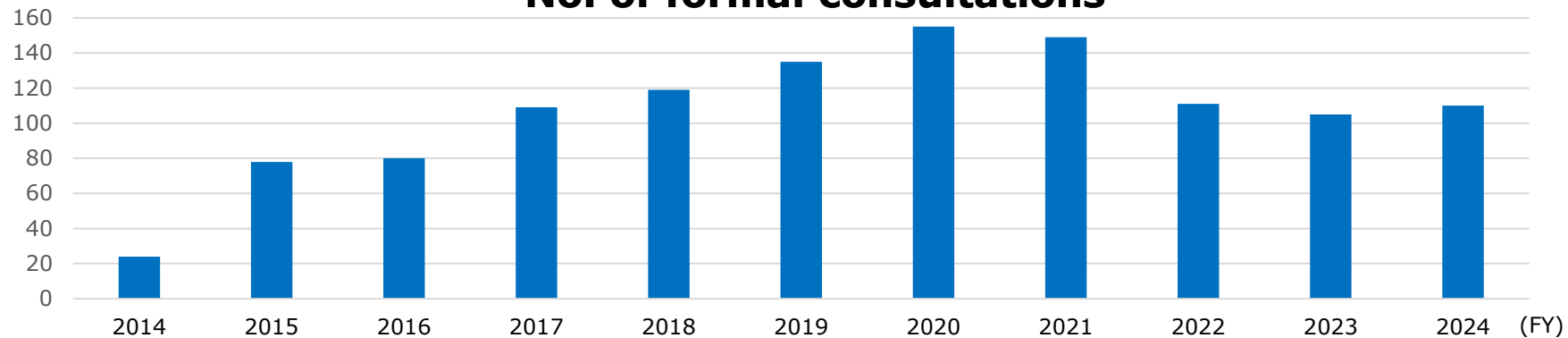


No. of Clinical Trial Notifications/consultations

No. of initial Clinical Trial Notifications



No. of formal consultations



<https://www.pmda.go.jp/files/000271121.pdf>
<https://www.pmda.go.jp/files/000265314.pdf>

The number of initial CTNs and consultations were increased dramatically when the PMD Act was enacted, and they have remained constantly high for the last decade.



Orphan Designation

- Objective

To promote the R&D of the products for rare diseases to provide the patients with safe and effective products as early as possible

- Criteria for designation Notification in English: <https://www.pmda.go.jp/files/000268408.pdf>

1. Number of patients (< 50,000 patients in Japan or one of [the designated intractable diseases](#))
(in Japanese)

2. Medical needs (Serious diseases with high medical needs)

3. Possibility of development

- Incentive (underlines; PMDA-related)

- Grant-in-Aid for R&D of orphan designated drugs
- Tax deduction for R&D expenses
- Priority scientific consultation
- Priority review (9 months); compared to 12 months for standard)
- Premium drug pricing
- Extension of re-examination period



SAKIGAKE Designation

- Objective

To put innovative products into medical practice faster in Japan

- Criteria for designation Notification in Japanese: <https://www.pmda.go.jp/files/000240376.pdf>

1. Innovativeness - New mode of action (in principle)

2. Severity of target disease - Life-threatening or no curative therapies available

3. Prominent efficacy - No existing therapies, or probable significant improvement in efficacy or safety compared to existing therapies

4. Plan/System - Submit the Marketing authorization application (MAA) in Japan first or at the same timing (within 3 months) as the first MAA submission in other regions

- Incentive (underlines; PMDA-related)

- Concierge service offered by senior review partner

- Priority scientific consultation

- Pre-assessment in consultation

- Priority review (6 months; compared to 12 months for standard)

- Premium drug pricing

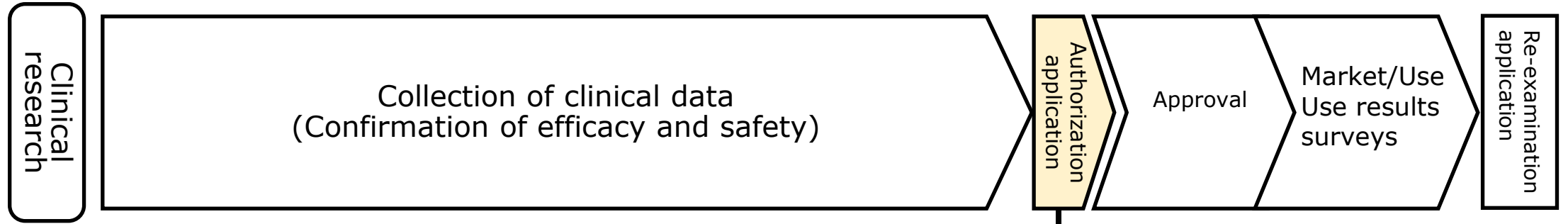
- Extension of re-examination period



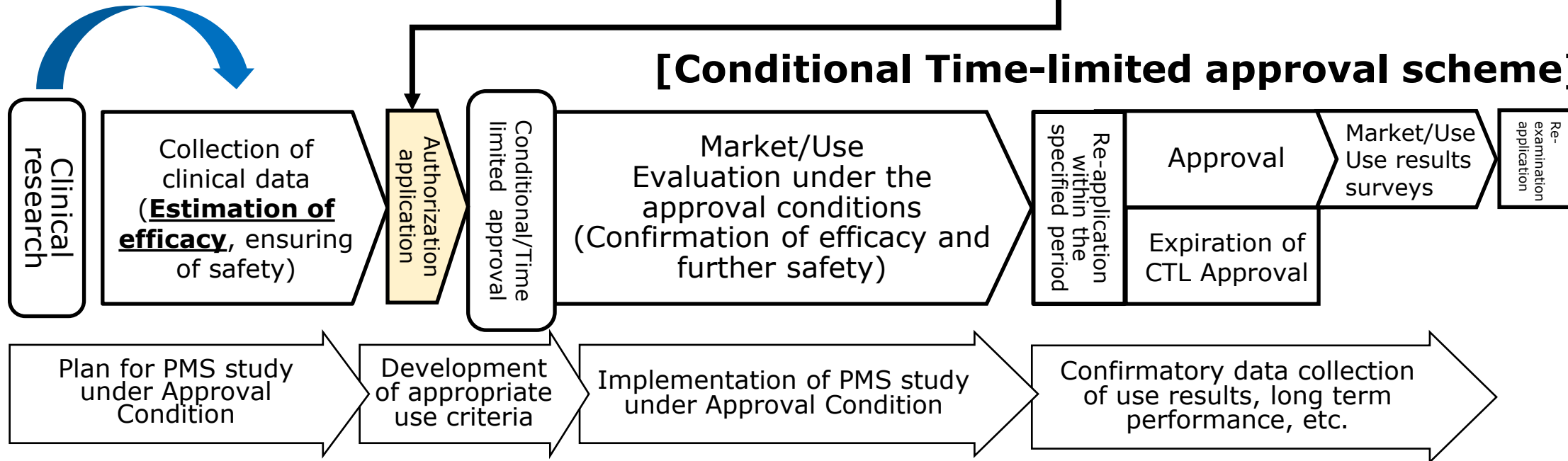
Conditional and Time-limited Approval Scheme

[Conventional approval scheme]

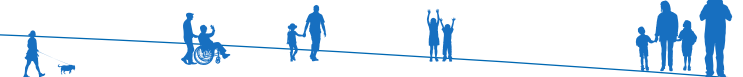
(CTL Approval Scheme)



[Conditional Time-limited approval scheme]



Modified from Maruyama et al., Adv Exp Med Biol, 1430, 155-179 (2023)



CTL Approval Scheme: Legal Basis

Conditional and Time-Limited Approval

Article 23-26

https://www.japaneselawtranslation.go.jp/ja/laws/view/3213#je_ch6at7

- (1) When an item that the applicant for approval prescribed in paragraph (1) of the preceding Article intends to market is a regenerative medicine product which falls under all of the following items, the Minister of Health, Labour and Welfare may grant approval prescribed in paragraph (1) of the same Article for such item by providing necessary conditions for the appropriate use of the item with a period not exceeding seven years, notwithstanding the provisions of paragraph (2), item (iii), (a) and (b) of the same Article, after obtaining opinions from the Pharmaceutical Affairs and Food Sanitation Council:
- (i) the regenerative medicine products pertaining to the application have heterogeneity;
 - (ii) the product is predicted to have the proposed indication or performance in the application;**
 - (iii) It should not be predicted to be of no value for use as a regenerative medical product due to its markedly adverse effects compared with the indication or performance of the application;
- (2) When the Minister of Health, Labour and Welfare confirms that it is especially necessary to conduct an examination under paragraph (2), item (iii) of the preceding Article pertaining to an application prescribed in paragraph (5), the Minister of Health, Labour and Welfare may extend the period not exceeding three years from the period prescribed in the preceding paragraph after obtaining opinions from the Pharmaceutical Affairs and Food Sanitation Council.
- (3) A person who has received approval prescribed in paragraph (1) of the preceding Article provided with conditions and time-limits pursuant to the provisions of paragraph (1) must conduct an investigation on the results of usage and other investigations for regenerative medicine products specified by Order of the Ministry of Health, Labour and Welfare, and report the results of the investigations to the Minister of Health, Labour and Welfare pursuant to the provisions of Order of the Ministry of Health, Labour and Welfare.



Guidance for CTL Approval for Regenerative Medical Products and the Development of subsequent Efficacy Evaluation Plan

<https://www.pmda.go.jp/files/000274350.pdf> (in English) (29 March 2024)

Provisional Translation (as of March 2025)*

PSB/MDED Notification No.0329-3
March 29, 2024

To: Directors of Prefectural Health Departments (Bureaus)

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

Guidance for Conditional and Time-Limited Approval for Regenerative Medical Products
and the Development of Subsequent Efficacy Evaluation Plan

Act on Securing Quality, Efficacy and Safety of Products Including Pharmaceuticals and Medical Devices (PMD Act) provides conditional and time-limited approval for regenerative medical products to ensure safety and to seek rapid practical application (Article 23-26). Four products have been approved through conditional and time-limited approval scheme.

With the aim of increasing predictability of the application for the conditional and time-limited approval scheme and promoting the further development of regenerative medical products, the "Guidance for Conditional and Time-Limited Approval for Regenerative Medical Products and the Development of Subsequent Efficacy Evaluation Plan" has been compiled as attached. Please notify the related organizations under your jurisdiction of this Notification to utilize as a reference for the development of regenerative medical products.

In addition, the copy of this notification is released to related associations and Pharmaceuticals and Medical Devices Agency (PMDA).

- To further enhance the development of regenerative medical products by improving the predictability of CTL approval
- Content
 1. Background
 2. Objective
 3. Scope
 4. Points to be considered for the review of CTL approval for regenerative medical products and assessment of the plan for post-marketing approval condition assessment

Also refer to "Guidance on Conditional and Time-Limited Approval for Human Cell-Processed Products Derived from Mesenchymal Stem Cells or Mesenchymal Stromal Cells of Human Origin and Evaluation for Subsequent Efficacy Evaluation Plan" <https://www.pmda.go.jp/files/000274351.pdf> (in English)(29 March 2024)



Handling of the Conditional and Time-limited Approval for Regenerative Medical Products

<https://www.pmda.go.jp/files/000278074.pdf> (in English) (6 October 2025)

厚生労働省医薬局医療機器審査管理課長

(公 印 省 略)

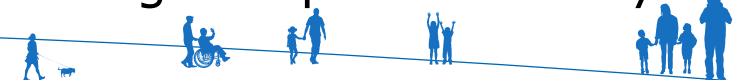
再生医療等製品の条件及び期限付承認の取扱いについて

再生医療等製品については、安全性を確保しつつ、迅速に実用化が図られるよう、医薬品、医療機器等の品質、有効性及び安全性の確保等に関する法律（以下「法」という。）第23条の26において、条件及び期限付承認制度（以下「本制度」という。）が設けられました。これまでも、状況に応じて個別に検討し、検証的臨床試験の成績を求めることなく、製造販売後に必要な調査等を実施することを承認条件として当該再生医療等製品の製造販売承認を行ってきたところです。また、本制度の運用等については、「再生医療等製品に係る条件及び期限付承認並びにその後の有効性評価計画策定に関するガイダンス」（令和6年3月29日付け医薬機審発0329第3号厚生労働省医薬局医療機器審査管理課長通知）（以下「ガイダンス」という。）等に示したところです。

独立行政法人医薬品医療機器総合機構（以下「PMDA」という。）で実施している対面助言や承認審査における経験を踏まえ、条件及び期限付承認に関する対面助言等での頻出の相談事項を抽出し、製造販売承認申請（以下「承認申請」という。）の手續等について、下記のとおり取り扱うこととしましたので、御了知の上、貴管下関係団体、関係機関等に周知徹底を図るとともに、適切な指導を行い、その適正な運用に努められるようお願いいたします。

なお、本通知により、これまでの再生医療等製品の承認申請に必要な申請資料等の取扱いを変更するものではないことを申し添えます。

- To clarify the procedures of the CTL Approval Scheme based on accumulated experience through consultation and assessment
- Content
 1. Procedures for CTL Approval
 - (1) Pre-application consultation
 - (2) 1-1 Application intended for the CTL Approval Scheme and its review
 2. Procedures after the CTL Approval
 3. Procedures of Application after the CTL Approval
 4. Basic approach regarding the utilization of the CTL Approval Scheme and Japanese clinical data in cases where clinical trials of regenerative medical products for rare diseases, etc. have been conducted only overseas
 5. Concept of quality control strategy throughout product Lifecycle



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PMDA's International Offices



Asia Office, Bangkok



PMDA Central Office, Tokyo



Washington D.C. Office

Establishment of PMDA's international hubs to enhance international contribution/capability for regulatory proposal



General Consultation Service at Washington D.C. Office

[Application for General Consultation](#)



The screenshot shows the PMDA website interface. At the top, there is a search bar and navigation links for 'PMDA', 'About PMDA', and 'Formats DL'. Below this is a 'Safety Alert & Recalls/ Review Reports/ Package Inserts etc.' notification. The main navigation menu includes 'Menu of each service', 'Menu for each of you', and 'Menu of each product type'. The 'Menu of each service' section lists: 'Reviews and Related Services', 'Post-marketing Safety Measures', 'Relief Services for Adverse Health Effects', 'Regulatory Science/The Science Board/Standard Development', and 'International Activities'. The breadcrumb trail reads: 'Home > International Activities > Overseas Office > PMDA Washington D.C. Office > PMDA Washington D.C. Office General Consultation Service'. The main content area is titled 'PMDA Washington D.C. Office General Consultation Service' and includes buttons for 'Add this page to "Favorite pages"' and 'Print the text'.

Start-up companies in U.S.

Application by e-mail

**PMDA
Washington D.C. Office**

Free of Charge Consultation

【Pharmaceutical affairs
-related cases】

**PMDA
Tokyo HQ**

For advice on
individual products,
Review Teams in
HQ will take over

【Non Pharmaceutical affairs
-related cases】

Contact points according
to
consultation contents

- Guide for better understanding PMD Act
- Provide initial general comment on Japanese regulatory information to U.S. start-up companies
- Support procedures for formal consultation at PMDA Tokyo Office



PMDA Asian Training Center



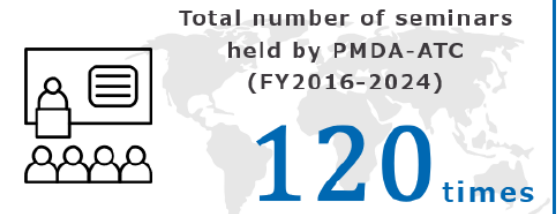
- Established in 2016
- contribute to universal health coverage in Asia through regulatory harmonization in the Asian region from capacity building

2016 – 2024

Participated from **76** countries/regions

All Participants **3,559** / Participants from Asia **3,067**

PMDA-ATC in numbers



PMDA-ATC Review of CGTPs Seminar 2025 for South-East Asian countries (15-17, July 2025)



Comments from the participants:

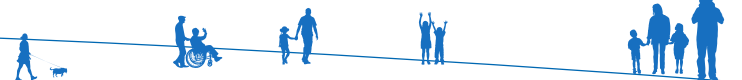
"I find the case studies interesting and so much I have learned from there."

"This seminar helped me deepen my understanding on CGTPs and learned key points for consideration in reviewing CGTPs in my home country."

"I will apply the knowledge from the seminar to develop CGTP guidelines on registration."

"As we have on-going review of a CGTP application, this seminar helped me to see the bigger picture of the evaluation of CGTPs."

<https://www.pmda.go.jp/english/symposia/0338.html>

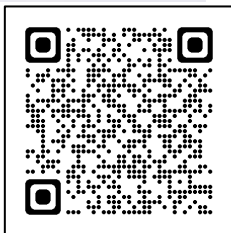


Where to Find Information?

Regenerative Medical Products

2. Approved Regenerative Medical Products

- [List of Approved Products](#)
- [Review Reports](#)
- [Revisions of PRECAUTIONS](#)



3. Support to Venture Companies

- [PMDA's Support to Venture Companies \[2.1MB\]](#)
- [Doing business in Japan: What is attracting? \[1.4 MB\]](#)
- [Supports from Japanese government \(MHLW\)](#)

4. Related Guidelines and Notifications for Regenerative Medical Products

Marketing authorization application (MAA)

- Questions and answers (Q&A) on release testing of the imported regenerative medical products, PSB/MDED, PSB/CLD Administrative Notice, 2024. [[Japanese \[144KB\]](#)] [[English \[143KB\]](#)]
- Guideline for comparability of human cell-processed products subject to changes in their manufacturing process, PSB/MDED Notification No. 0329-1, 2024. [[Japanese \[431KB\]](#)] [[English \[245KB\]](#)]

Good tissue practice (GTP)

- Standards for biological raw materials, MHLW Notification No. 210, 2003. [[Japanese \[315KB\]](#)] [[English \[73KB\]](#)]

Making everyone's lives brighter together

Review Reports: Regenerative Medical Products

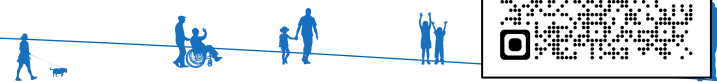
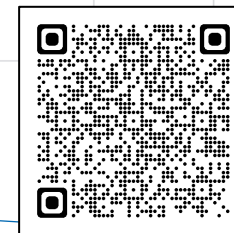
A

Brand Name	Non-proprietary Name	Approved In	English	Japanese
Abecma Initial Approval	Idecabtagene vicleucel	January 2022		
Abecma Partial Change Approval	Idecabtagene vicleucel	December 2023	English [607.25 KB]	Japanese [847.24 KB]
Alofisel	Darvadstrocel	September 2021		

[Back to Top](#)

B

Brand Name	Non-proprietary Name	Approved In	English	Japanese
Breyanzi Initial Approval	Lisocabtagene maraleucel	March 2021		
Breyanzi Partial Change Approval	Lisocabtagene maraleucel	December 2022		



For development in Japan



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

<https://www.pmda.go.jp/english/int-activities/industry/0001.html>



Safety Alert & Recalls/ Review Reports/ Package Inserts etc.



Formats DL

International Activities

For Industry - for development in Japan



Add this page

For Industry

for development in Japan

1.Overview



2.Regulations and Services of PMDA



3.Information for Approved Products in Japan



4.Procedures in Japan



5.Advanced Efforts



6.Links



Where to meet PMDA staff members in-person?

- Global Bio Conference 2026, Seoul, 26-28 August, 2026



- ISCT ASIA 2026, Singapore, 2-5 September, 2026



- CELL & GENE MEETING ON THE MESA, 5-7, October, 2026



Summary

- Regenerative Medicine is regulated by two Act. (the Safety Act and the PMD Act) in Japan.
- Twenty-six (26) regenerative medical products are currently approved under the PMD. Act in Japan.
- The development of regenerative medical products has been encouraged by several measures (e.g., Orphan designation, SAKIGAKE designation, and Conditional and Time-limited Approval scheme) in Japan.
- The PMDA is actively strengthening collaboration with international regulatory authorities and further expanding outreach initiatives to facilitate the development of RMPs in Japan and globally.



Thank you for your attention!



Making everyone's lives brighter together

Acknowledgements

Colleagues in the Office of Cellular and Tissue-based Products, PMDA

