PMDA's Activities Leading to Medical Device Innovation

Pharmaceuticals and
Medical Devices Agency

https://www.pmda.go.jp/english/index.html

Key points for your development strategy in Japan

<Japan's Advantage>

- **2nd largest market** of Medical Devices
- **ALL citizens (125 Mil.) are covered by NHI**
- **All medical devices are covered by the NHI in principle** and **no HTA** before the inclusion
- Regulations are harmonized internationally
- Hospitable support for venture companies

A Key for World-Wide Development of Medical Products!

PMDA's Performance

1. Strategy Consultation
2. High Predictability of Review Process
3. Internationally Harmonized Regulations
4. PMDA Outreach

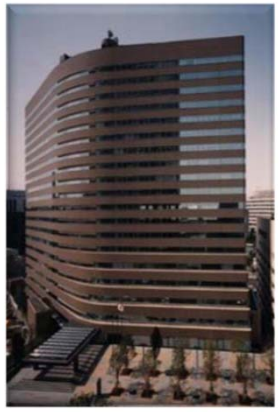
Introduction of PMDA

- Pharmaceuticals and Medical Devices Agency (PMDA) is a Government Affiliated Organization in Japan.
- PMDA is responsible for scientific review and consultation of medical products to be approved in Japan.

Hokuriku Branch

Toyama

Main office



Kansai Branch

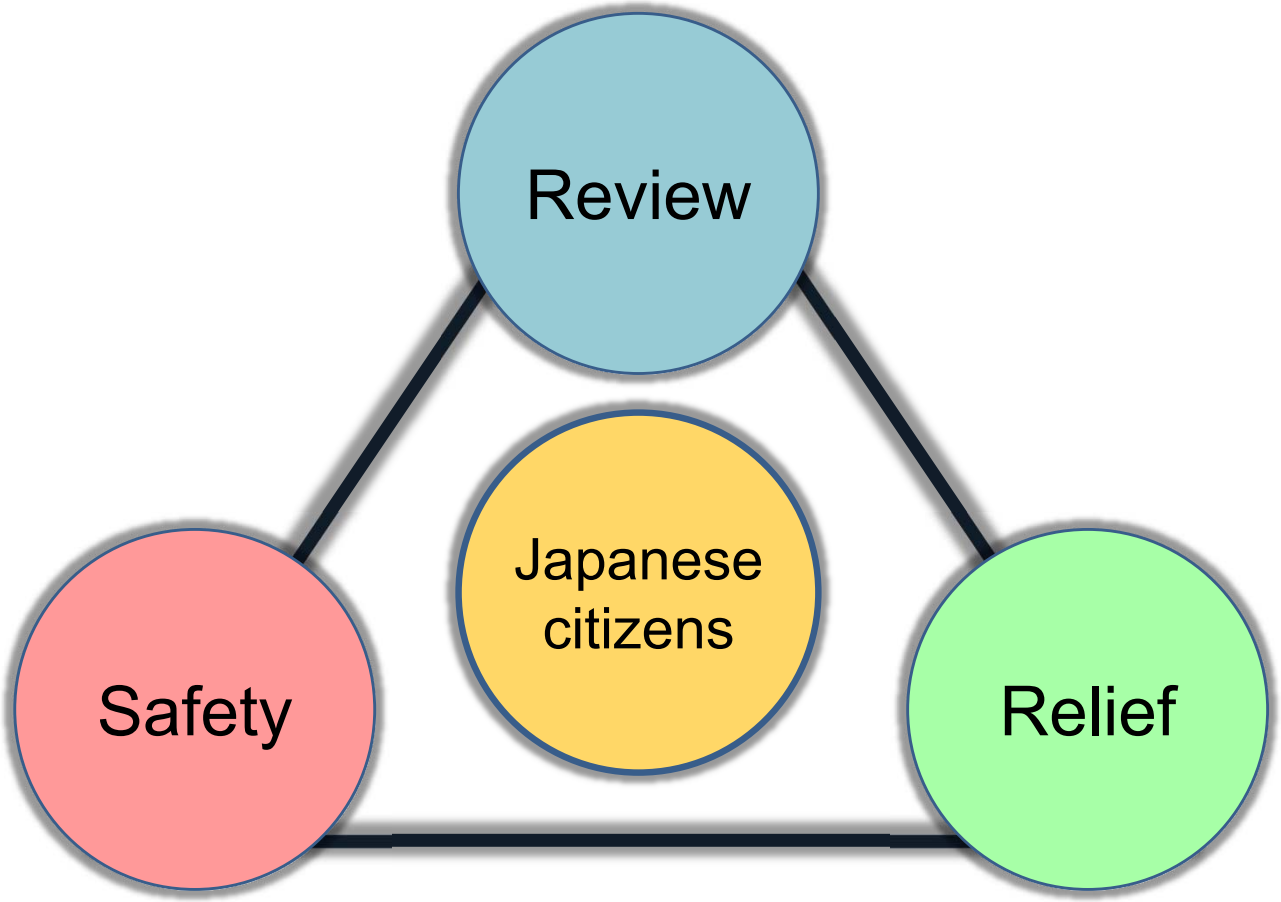
Tokyo

Osaka

Established on April 1, 2004

Three-pillar System Unique to Japan

- PMDA's mission is to help improve public health through Three-pillar system; (1) Relief Services, (2) Product Reviews, and (3) Post-marketing Safety Measures.

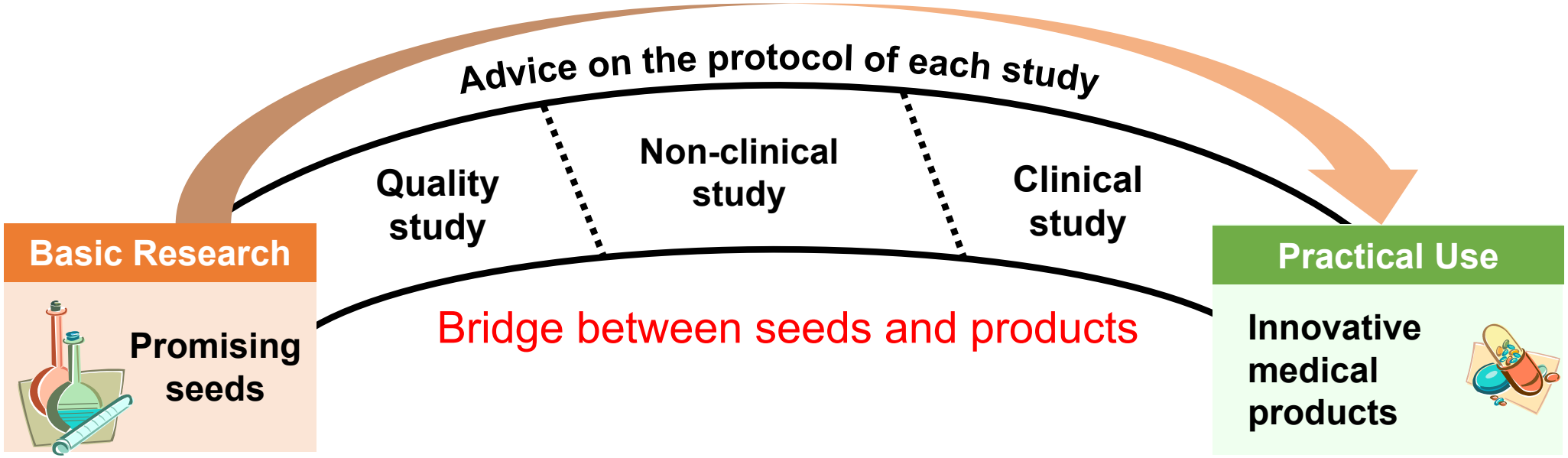


1. Strategy Consultation

- Develop strategic plan in Japan -

Regulatory Science Consultation on R&D Strategy

- PMDA supports the establishment of an exit strategy via Regulatory Science (RS) Consultation on R&D Strategy.
- Facilitate the development of medical products by developing a more reliable roadmap.
- Accelerate the clinical trials led by academia.



Outline of the RS Consultation

■ Each consultation is offered through online or in-person.

Category	Objective	Consultant	Period from application to consultation	Duration	Fee	Minutes
General Consultation	Introduction of general information on: • Consultation system • Pharmaceutical regulatory system • Related guidelines	Technical Experts	1 to 3 weeks	20min	Free	Not shared
Pre-consultation meeting	Clarification of discussion points, consultation dossiers	Technical Experts and Reviewers	2 to 5 weeks	30min	Free	Not shared
Consultation	Scientific discussion	Technical Experts and Reviewers	2 to 3 months	Max. 2hr	Charged	Shared

Please contact:

rs-contact@pmda.go.jp

PMDA offers 90% discount to venture companies.

Prerequisites for Fee Reduction in RS Consultation

- Following prerequisites have to be fulfilled by venture companies.

✓ An SME (Small and Midsize Enterprises*)

* employees < 300 or company's capital < JPY 300M

✓ Another corporate body does not hold shares or capital contributions equivalent to 1/2 or more of the total number of shares or the total amount of contributions.

✓ Two or more corporate bodies do not hold shares or capital contributions equivalent to 2/3 or more of the total number of shares or the total amount of contributions.

✓ Net profit is not recorded or is recorded without business revenue in the previous fiscal year.

Other support programs in Japan
1. MEDISO (MEDical Innovation Support Office)

- MEDISO provides support for venture companies, academia, and individuals intending to put into practical use the pharmaceuticals, medical devices, and regenerative medicinal products.
- Support is via online meeting or e-mail.
- Experts in R&D, consultants in pharmaceutical affairs, and experts from related organizations including the Ministry of Health, Labour and Welfare are in cooperation.
- Services are free of charge.

MEDISO consultation is available free of charge !!!

mediso@ml.mri.co.jp

Other support programs in Japan
2. CRCHs (Clinical Research Core Hospitals)

- CRCH plays a central role in international-standard clinical research to promote the development of innovative pharmaceuticals and medical devices originating in Japan.

- Abundant experience in:

✓ Planning, implementation, and analysis of clinical research and trials
✓ Commercialization of innovative seeds

- Diverse human resources:

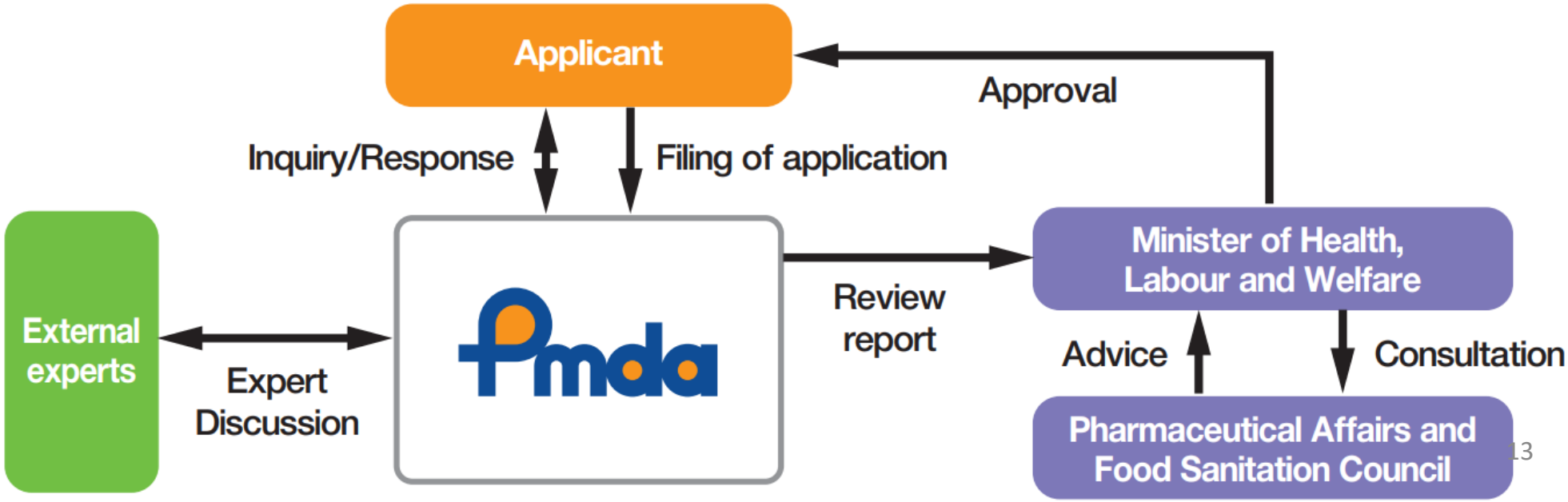
✓ Experts in clinical research and commercialization
✓ Cooperation from various departments in the hospitals
✓ Biostatisticians and data managers
✓ CRC and other operational units
✓ Review committee bodies such as CRBs
✓ Staff experienced in PMDA

- National Cancer Centre Central Hospital
- Tohoku University Hospital
- Osaka University Hospital
- National Cancer Centre East Hospital
- Nagoya University Hospital
- Kyushu University Hospital
- University of Tokyo Hospital
- Keio University Hospital
- Chiba University Hospital
- Kyoto University Hospital
- Okayama University Hospital
- Hokkaido University Hospital
- Juntendo University Hospital
- Kobe University Hospital
- Nagasaki University Hospital

2. High Predictability of Review Process

Regulatory Submission and Approval Process

- In the medical device review process, review team reviews the data submitted for a product.
- During the process, the reviewers exchange opinions with external experts to enable more highly specialized reviews.
- Could be approved without Clinical Evidences or with Registry Data.



Medical Device Classification and Regulation

- MDs are classified into 4 categories (Class I to IV) according to their risk level.
- Pre-market regulatory process for MDs differs depending on the classification.
- Some MDs, not subject to PMDA review, are required to be certified by MHLW registered certification bodies before marketing.

Risk Level	Low → High			
International Classification *	Class I	Class II	Class III	Class IV
Classification under PMD Act	General Medical Devices	Controlled Medical Devices	Specially Controlled Medical Device	
Regulation	Notification to PMDA	Certification by registered certification bodies	Approval by the Minister of MHLW (based on scientific review by PMDA)	
Specific Description	Devices that may pose an extremely low risk to the human body in case of a malfunction Examples: ● In vitro diagnostic devices ● Steel made small devices (including a scalpel, tweezers) ● X-ray film ● Devices for dental technique	Devices that may pose a relatively low risk to the human body in case of a malfunction Examples: ● MRI system ● Electronic endoscope ● Ultrasonic system ● Dental alloy	Devices that may pose a relatively high risk to the human body in case of a malfunction Examples: ● Dialyzer ● Bone prosthesis ● Automated external defibrillator (AED) ● Mechanical ventilator	Devices that are highly invasive and thus may pose a life-threatening risk in case of a malfunction Example: ● Pacemaker ● Artificial cardiac valve ● Artificial breast ● Stent graft

* Classes I – IV correspond to GHTF categories (Class A – D)

Medical Device Review Times

- PMDA to ensure a more predictable review process, aiming to achieve the review time of 14 months for new medical devices, and 10 months for priority review.

Total Review Time for New Medical Devices (Standard Review Applications)

	FY 2018	FY 2019	FY 2020	FY 2021	FY 2022
percentile	**80th**	**80th**	**80th**	**80th**	**80th**
Total review time	**12.0**	**11.1**	**10.8**	**11.9**	**12.0**
Number of approved applications	**36**	**27**	**29**	**33**	**19**

Note1: Values indicate the data for approved applications that were filed in or after 2004

Total Review Time for New Medical Devices (Priority Review Applications)

	FY 2018	FY 2019	FY 2020	FY 2021	FY 2022
percentile	80th	80th	80th	80th	80th
Total review time	**8.3**	**7.3**	**8.4**	**8.9**	**8.8**
Number of approved applications	2	3	2	1	2

Note1: Values indicate the data for approved applications that were filed in or after 2004

Accelerated Review Systems in Japan

■ Japan Offers Various Supporting Schemes for R&D Companies and Researchers.

Type	Area	Product features
Expedited review	**Any product categories**	In a particular situation requiring expedited review
Priority review		Designated as: 1. Orphan 2. Apparent improvement of medical care for severe diseases
SAKIGAKE (Forerunner designation)		• Innovative medical products • For serious diseases • Development & NDA in Japan: The NDA submission being the world's first or simultaneous with other countries • Prominent effectiveness expected based on non-clinical and early phase clinical study data
Conditional Approval	Drugs	Early application through confirmation of a certain degree of efficacy and safety in clinical trials other than confirmatory clinical trials
	Medical Devices	• High clinical needs • Balancing the pre- and post-market requirements
Conditional and Time-limited Approval	Regenerative Medical Products	• Based on the clinical data from the limited number of patients, efficacy is predicted in a shorter time compared with the conventional process. • Early-phase adverse reactions, etc. can be evaluated for safety in a short period of time.

SAKIGAKE (Forerunner Designation)

■ To put innovative products into medical practice in Japan.

<Requirements>

1. Innovativeness
2. Serious diseases
3. Prominent effectiveness
4. Applied first in Japan

<Incentives>

Concierge service offered by senior review partner (PMDA)

Priority scientific advice (PMDA)

Pre-review in consultation (PMDA)

Priority review (6 months)(PMDA)

Premium pricing

Fastest Practical Use in the world

Orphan Medical Device

- To promote R&D of the products for rare diseases to provide safe/effective products as early as possible.

<Designation Criteria>

1. Small number of patients
   < 50,000 in Japan or designated intractable disease
2. High medical needs
3. High probability of successful development

<Incentives>

*National Institutes of Biomedical Innovation, Health and Nutrition

Grant-in-Aid for R&D of orphan designated drugs (NIBIOHN*)

Tax deduction for R&D expenses

Priority scientific consultation (PMDA)

Priority review (PMDA)

Premium pricing

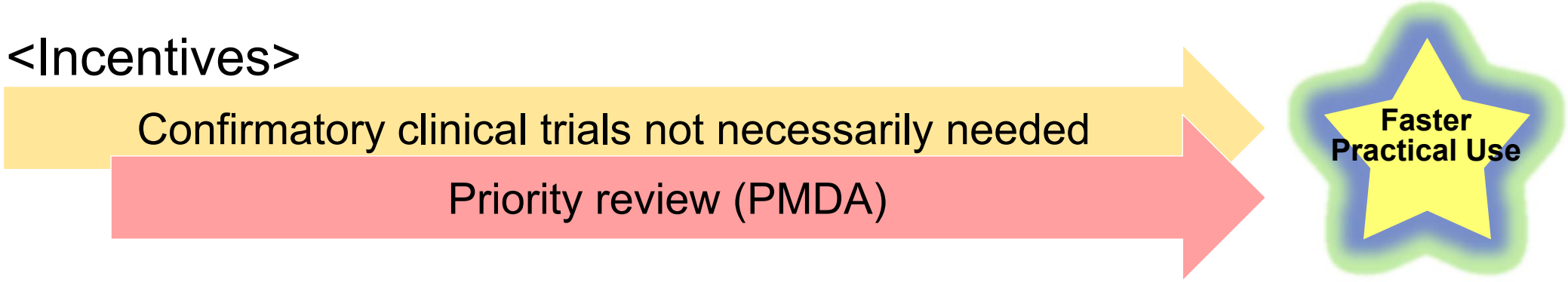
Conditional Approval

- Approved without conducting new trials on the condition that post-marketing risk management be carried out.

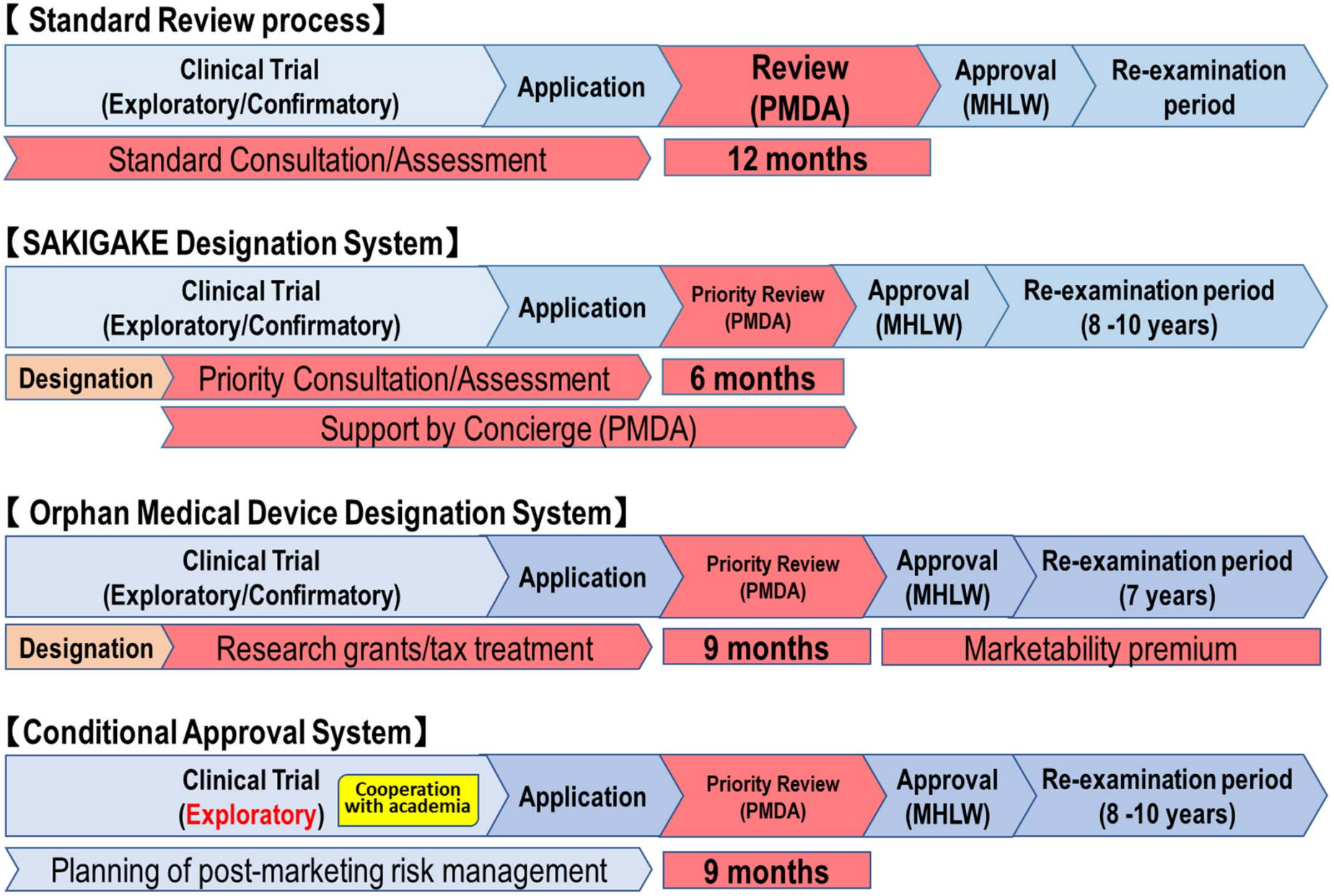
<Criteria>

1. Disease severity
2. Superior in efficacy or safety
3. Confirmatory clinical trials are not feasible
4. A certain degree of efficacy/safety is confirmed through other types of studies

<Incentives>



Development Flow (Clinical Trial to Post Market)



DX(Digital Transformation) Action Strategies in Healthcare for SaMD (DaSH for SaMD)

DASH for SaMD２（2023/9/6）

- Organize and publicize the two-step approval scheme for SaMD
- Develop guidelines for approval review and marketing procedures for SaMD for the general public
- Promotion of overseas acceptance of MHLW's review results (such as English translation of review reports)
- Subsidies for development funds for SaMD developers
- Support for SaMD developers to actively business overseas

DASH for SaMD（2020/11/24）

- Setup an office to review SaMD in MHLW and PMDA
- Establishment of SaMD centralized consultation service
- Next-generation medical device evaluation index, development guidance, audit points, and certification criteria formulation
- Trial implementation of priority review, etc. for innovative SaMD
- Promote the use of IDATEN (Improvement Design within Approval for Timely Evaluation and Notice) and streamline procedures, etc.

<Expand and continue>

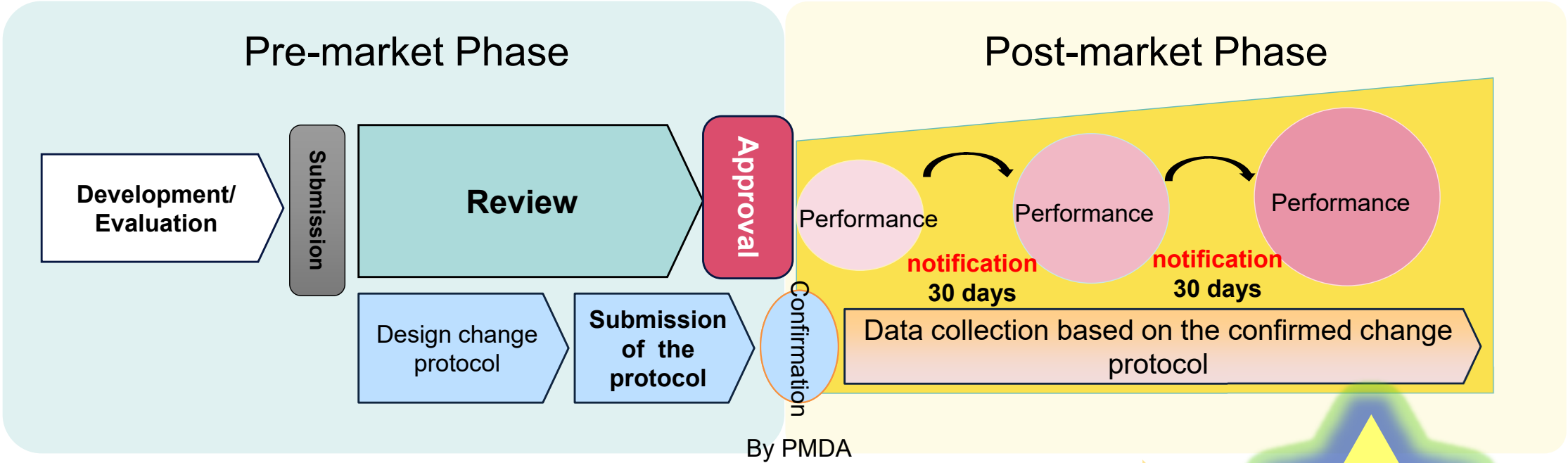
- Upgrade from office to Department for reviewing SaMD in PMDA
- Establishment of SaMD-specific consultation service
- (Continue)
- (Continue)
- (Continue)

Goals for the next 5 years

- Achieve early market introduction and establish clinical significance
- Expansion of more enhanced self-care options
- Promotion of better health for the public
- Exporting more and market acquisition of innovative SaMD developed in Japan
- Shorten the development cycle time of SaMD by contributing to a smooth and efficient market introduction
- Realization of efficient commercialization of SaMD
- Creation and early commercialization of innovative SaMD
- Smooth and efficient post-marketing performance improvement of SaMD

IDATEN （Improvement Design within Approval for Timely Evaluation and Notice）

- Post-Approval Change Management Protocol (PACMP).
- To enable continuous and timely improvements through product lifecycle. (suitable for SaMD. Could be applied to ALL Medical Devices.)



<Incentives>

No review Fee charged, in case the change request is as planned before the approval

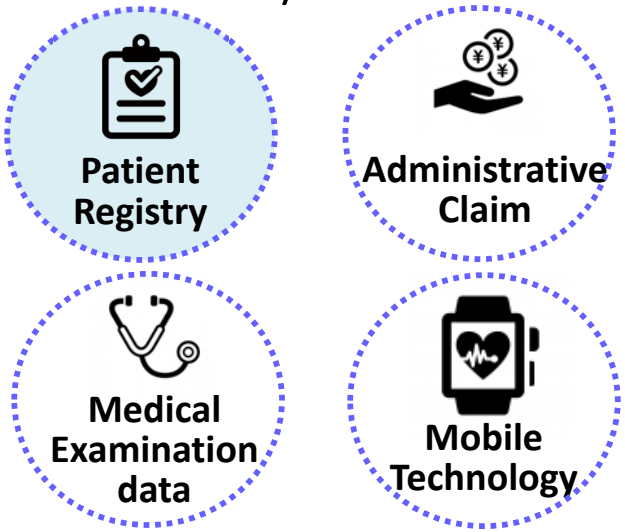
Smooth Change Management

Utilization of RWE to Evaluate Clinical Outcomes of Medical Devices

- Utilization of RWE through pre- and post-marketing phase is often effective for development of medical devices required repeating improvements and medical devices for orphan disease.

Source of RWD

- National / International
- Academic / Sponsor
- Procedure / Medical Device



Purpose of Utilization in regulatory use

1. **External control of clinical trials**
2. **Primary data or complement of clinical trials**
3. **Efficacy and/or safety evaluation of conditionally approved items**
4. **Post-marketing surveillance for safety measures**

Consultations for Development and Utilization of Registry

- PMDA has launched a new consultation categories about reliability of the registry data.

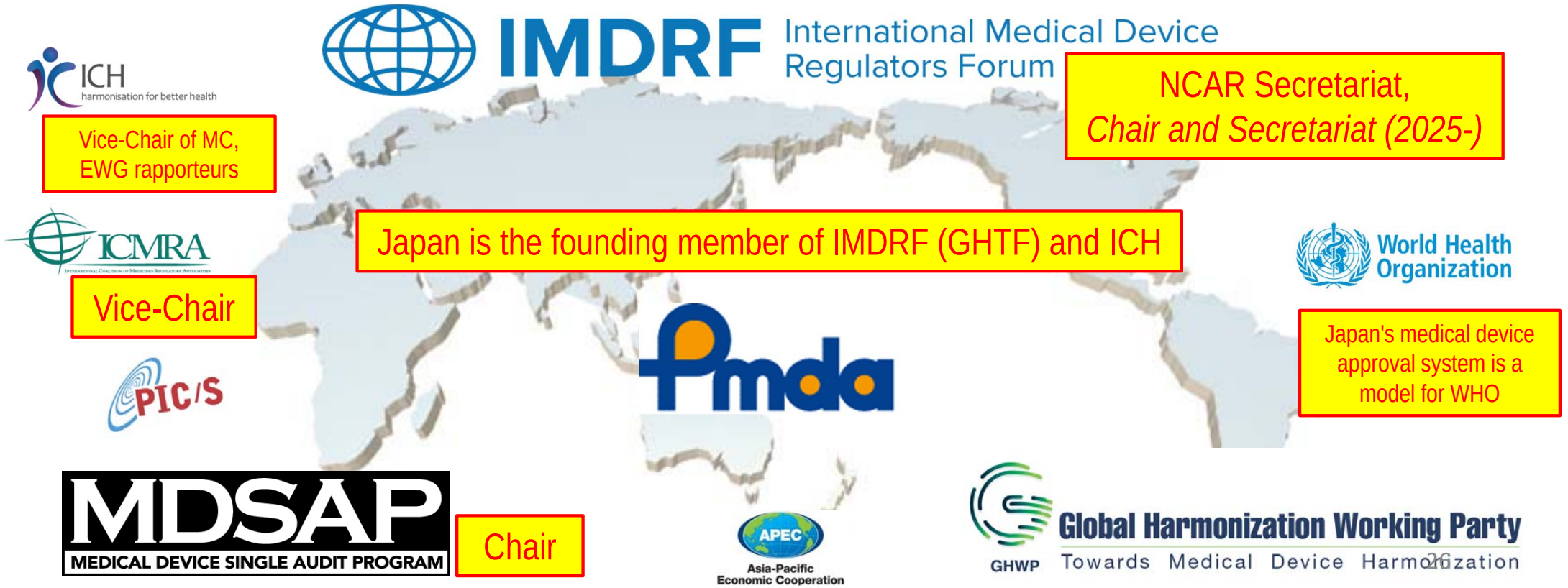
	Consultation Category	Consulter	Objective
1	**Development of Registry Data**	**Registry holder (mainly academic society)** 	- General consideration of development strategies for registry - Methods of ensuring the data reliability of registry for marketing approval/PMS applications
2	**Quality of Registry Data**	**Industry** 	- Check and specify the status of data reliability of registry for marketing approval/PMS applications corresponding to the individual new device

3. Internationally Harmonized Regulations

- Acceleration of International Development -

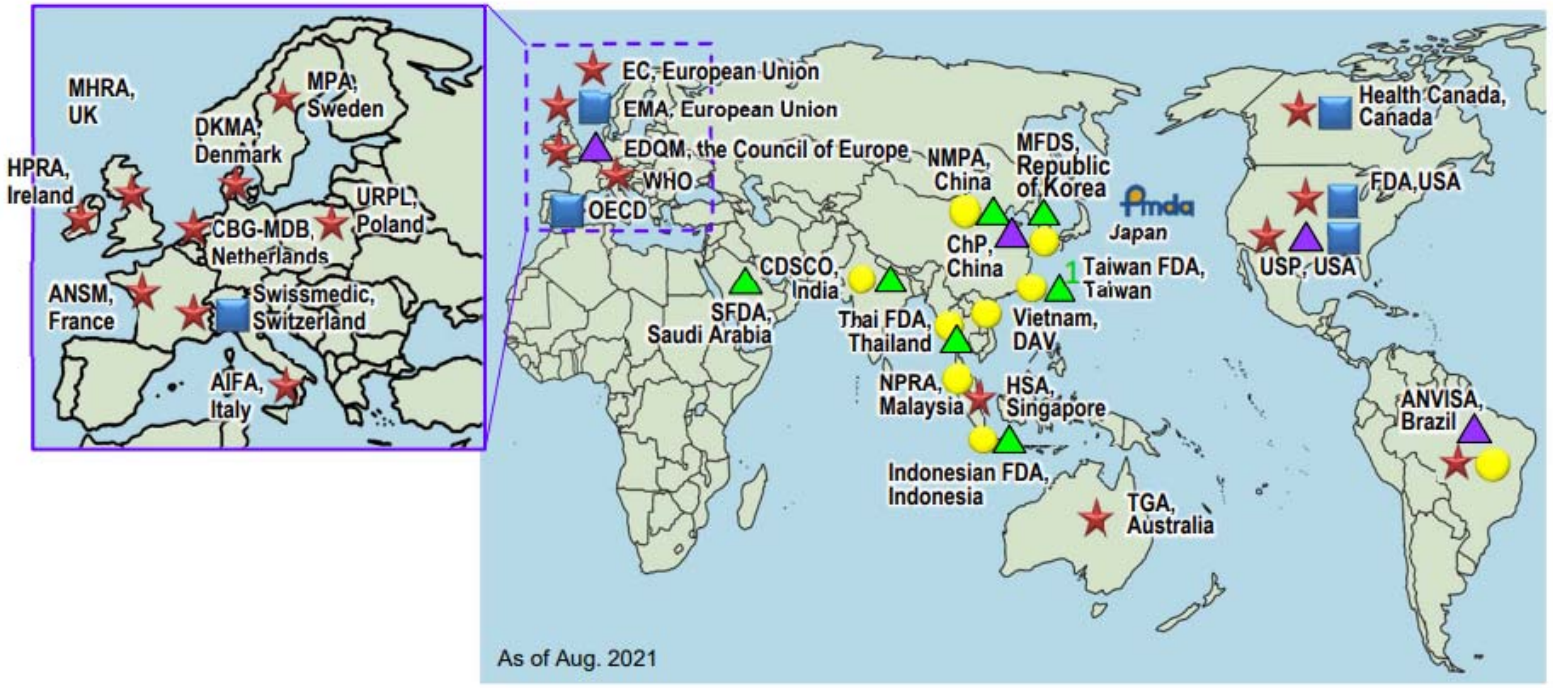
Multilateral Cooperation

- Cooperate with international harmonization frameworks for medical device regulations.
- Multilateral cooperation will support the expansion of medical devices into international market.



Bilateral Cooperation

- Promote regulatory reliance including review and post-market safety through bilateral cooperation between two countries.



Confidentiality Arrangement signed

Cooperative Arrangement signed

Joint symposium held

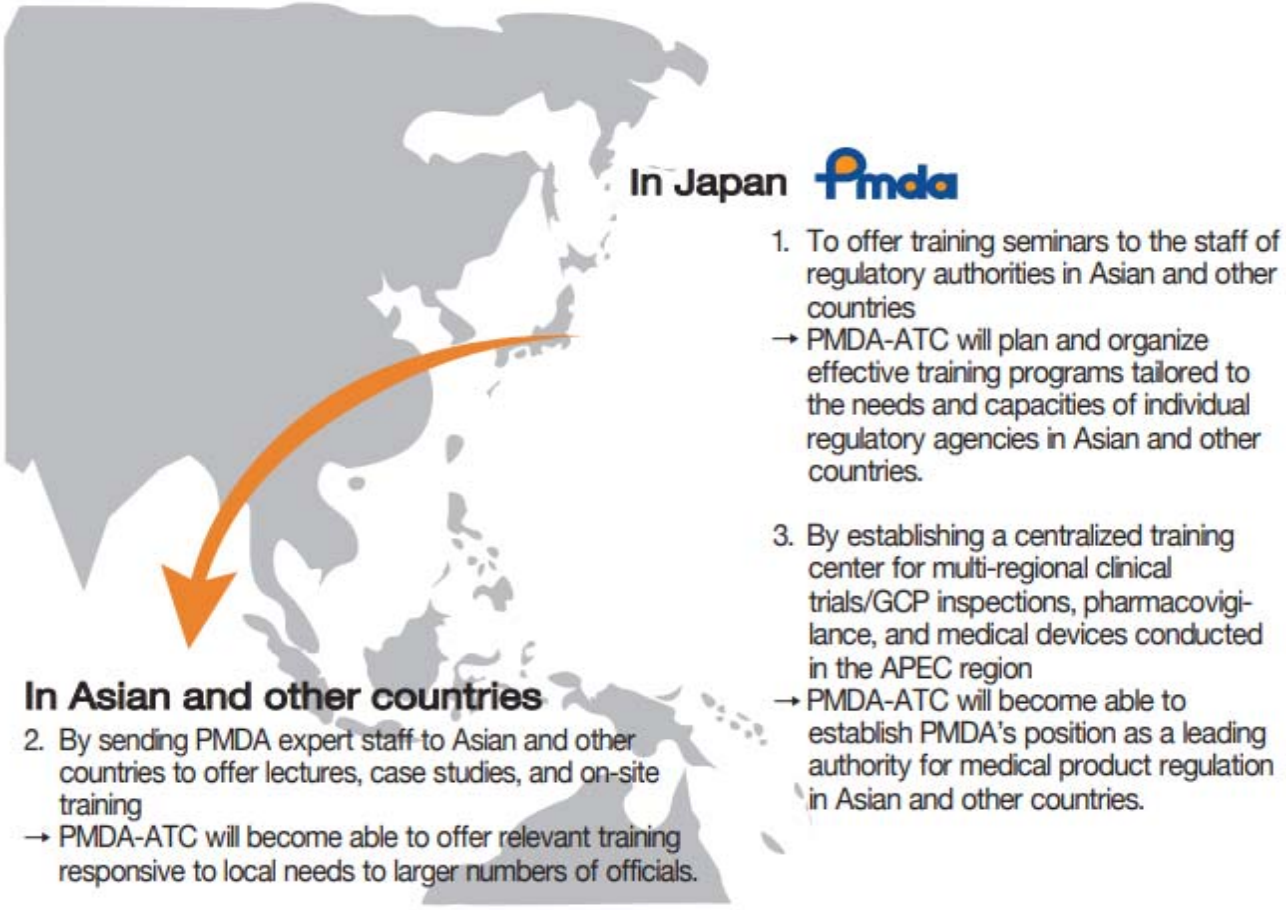
Cooperative Arrangement on cooperation of pharmacopoeia signed

PMDA staff stationed at the agency

1 Cooperative Arrangement signed between the Interchange Association of Japan and East Asia Relations of Taiwan

PMDA Asia Training Center (ATC)

- Promote greater understanding of internationally accepted regulations pertaining to pharmaceuticals and medical devices among regulatory authorities in Asian and other countries.



Examples of countries/regions which recognize Japan as reference country [As of September 2022]

Country/ region	System	Population* (million) (2022)	Medical Devices Market scale (billion USD) (2018**, 2020***,****)
Taiwan	• Reduction of documents on quality management systems for medical devices and IVDs (2018)	23.3	4.4***
Singapore	• Accelerated medical device and IVD review (2010)	5.6	2.0****
Malaysia	• Accelerated medical device and IVD review (2014)	32.6	1.4**
Mexico	• Accelerated medical device review (2012)	126.0	54.0**
India	• Acceptance of QMS investigation results in Japan for medical devices and IVDs (2015) • Exemption from conducting clinical trials in India (2017)	1417.2	48.9**
Australia	• Accelerated medical device and IVD review (2018)	25.8	4.6***
Thailand	• Accelerated medical device and IVD review (2019)	66.1	14.7**

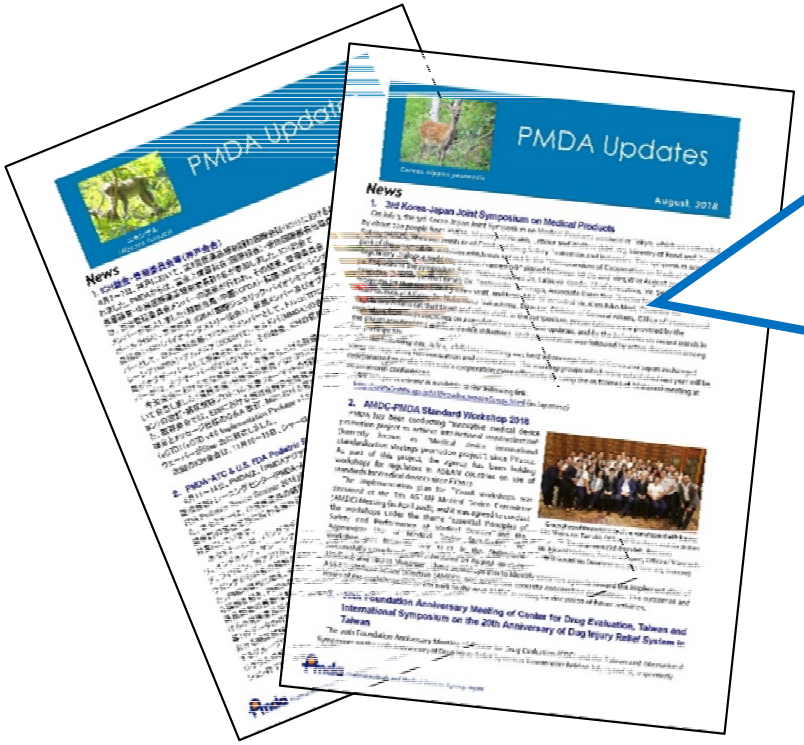
<Source>
* https://www.mofa.go.jp/mofaj/index.html ** https://healthcare-international.meti.go.jp *** https://www.trade.gov/ **** https://www.statista.com/

Not only providing review reports
PMDA supports these RAs by responding to their queries!

4. PMDA Outreach

Newsletter "PMDA Updates"

- Issued monthly via e-mail and on the PMDA website.
- Available in English and Japanese.
- Topics include international conferences (e.g., ICH, ICMRA, IMDRF, etc.), training seminars provided by PMDA-ATC and safety updates.



1. Events organized by PMDA
2. English Translation of Review Reports, Notifications and Administrative Notices
3. Monthly Safety Update
4. Planned International Conferences
5. Activities of PMDA staff stationed abroad

Email to: pmda_update@pmda.go.jp to subscribe to the newsletter!!

https://www.pmda.go.jp/english/int-activities/outline/0006.html

Further Information on PMDA

Further information can be found in the brochure on the PMDA website.

https://www.pmda.go.jp/files/000241469.pdf

QUESTIONS

Contact Us | Pharmaceuticals and Medical Devices Agency (pmda.go.jp)