Regulatory Update from PMDA – Japan

MIYASAKA Tomoyuki
Deputy Director of Medical Device Evaluation Division
Ministry of Health, Labour and Welfare
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IMDRF International Medical Device Regulators Forum

Legislation structure for Medical Products in Japan

Act	• Act on Securing Quality, Efficacy and Safety of Products Including Pharmaceuticals and Medical Devices (PMD Act, 1960)
Cabinet Ordinances	• Cabinet Ordinance on Act on Securing Quality, Efficacy and Safety of Products Including Pharmaceuticals and Medical Devices (1961) • Cabinet Ordinance on PAFSC (2000)
Ministerial Ordinances	• Ministerial Ordinance on Act (1961) • GCP for Medical device (2005) • GLP for Medical device (2005) • Good Vigilance Practice (GVP) • Quality Management System (QMS) ,etc.
Ministerial Notifications	• Essential principles • Certification criteria for Class II / III devices • Classification of medical devices • List of orphan designation, etc.
Notifications	• Information on application procedures • Guidelines for clinical evaluation ,etc.

Accelerated review systems in Japan

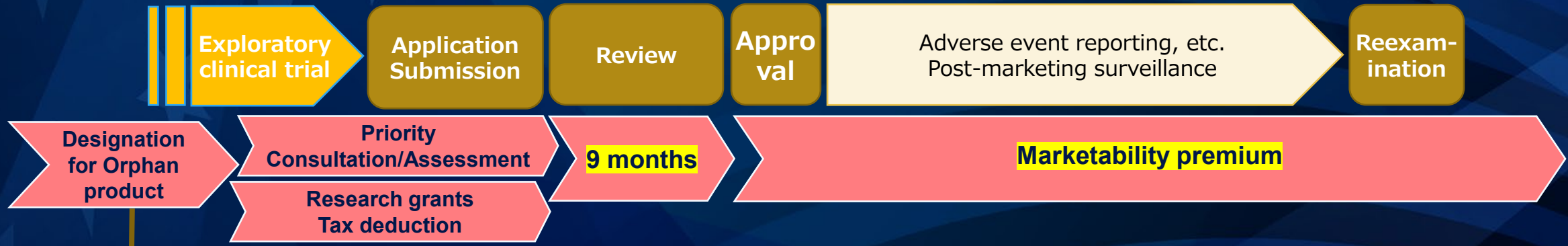
Government of Japan Offers Various Supporting Schemes for R&D Companies and Researchers.

Type	Area	Product features
(Expedited review)	Any product categories	In a particular situation requiring expedited review (voluntary measure by PMDA upon request of MHLW)
Priority review		Designated as: 1. Orphan Medical Devices 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 Early 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
Post-Approval Change Management Protocol (PACMP)	Medical Devices	• Predictability & Transparency in post-marketing change control

Orphan Medical Device Designation System

【Standard Review】

【Review for Orphan Medical Devices】

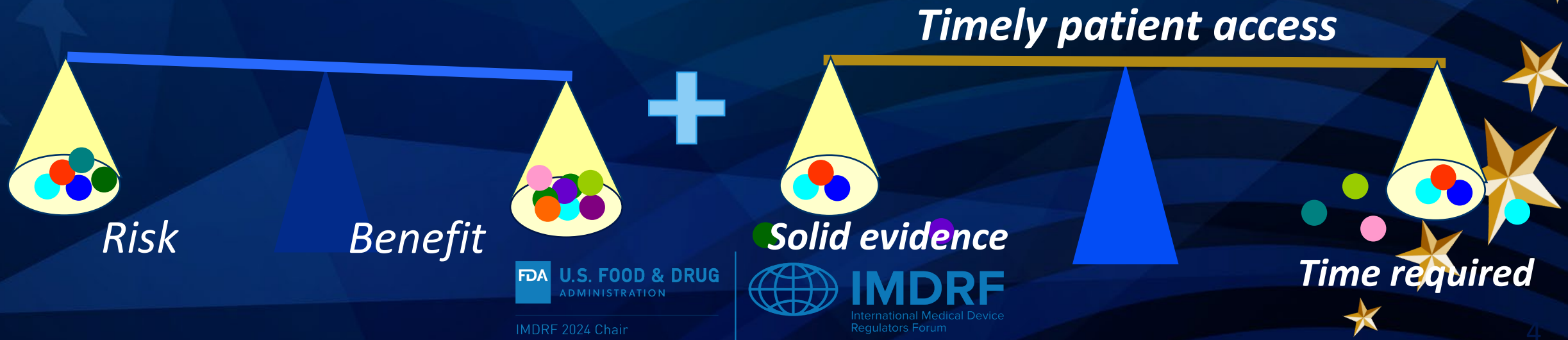


【Designation Requirements for Orphan Medical Devices】

1. Number of patients should be less than 50,000 in Japan (or designated intractable diseases).
2. High medical needs such as “No appropriate alternative medical intervention” or “High efficacy or safety is expected compared with existing products”.
3. High probability of successful development such as “Strong rationale to use the product for the target disease, and the appropriate development plan”.

Basic Concept of Regulatory Reviews in Japan

- The basic concept of regulatory review is to evaluate safety and performance based on the statement of intended use, which defines the characteristics of the device and the circumstances of its use, and to consider whether the balance of risks and benefits is appropriate.
- However, when it comes to innovative medical devices, if we try to evaluate them based on solid evidence, this means that we must accept that it will take a certain amount of time from development to marketing approval.
- On the other hand, many have recently called for a rethinking of the balance between timely patient access to medical devices and the time it takes to obtain more solid evidence, from a more patient-oriented perspective.
- In light of above situation, the Government of Japan has introduced some new systems for innovative medical devices to accelerate the patient access.



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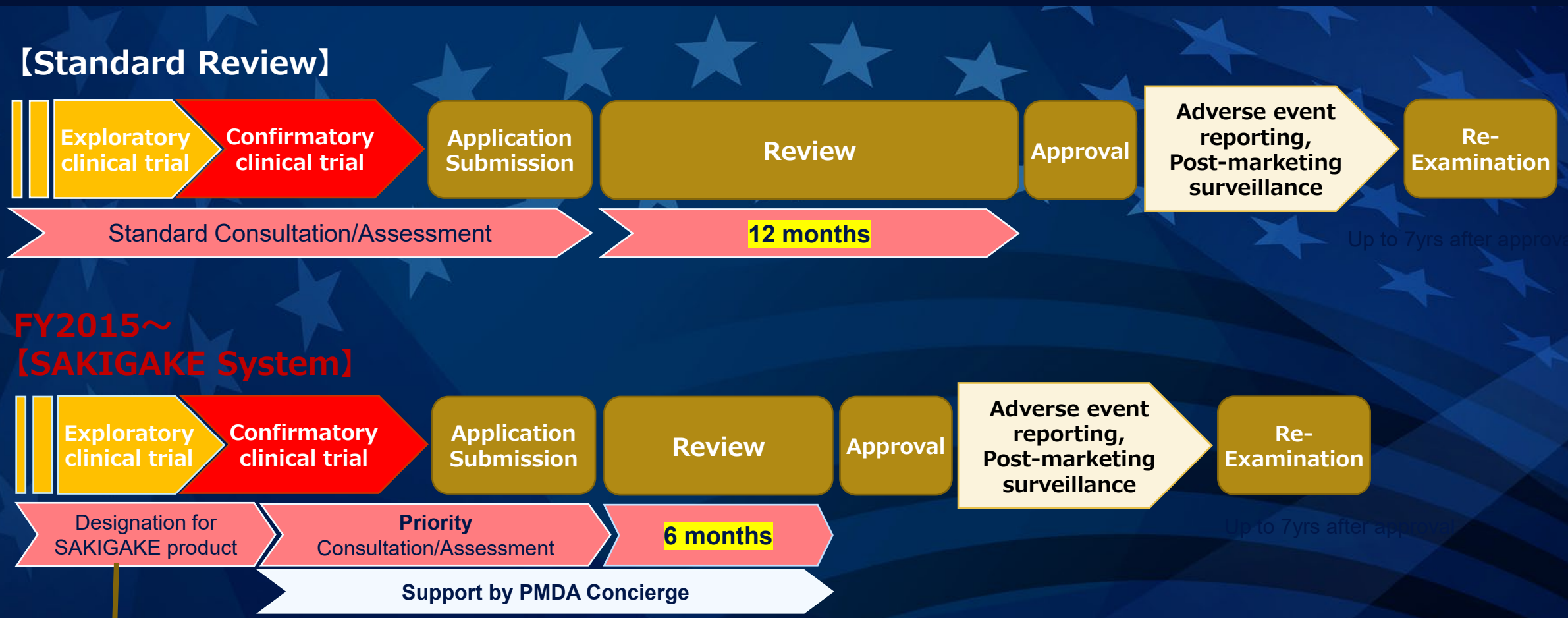
SAKIGAKE（Forerunner designation）



【Designation Requirements for SAKIGAKE】

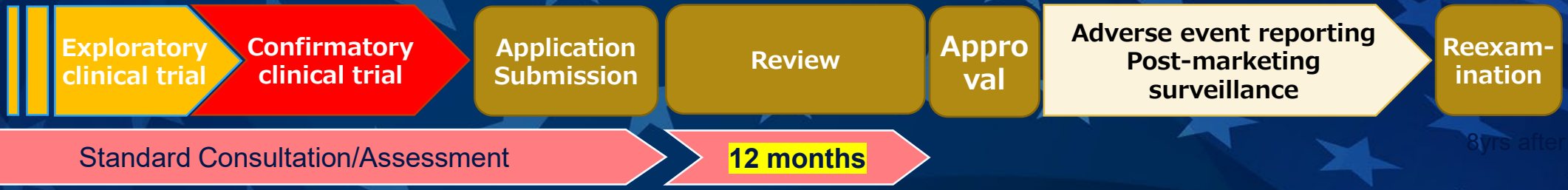
1. Epoch-making nature of the therapeutic or diagnostic method
2. Severity of the target disease
3. Extremely high efficacy or safety related to the target disease
4. Willingness and system for early development and submission for approval in Japan ahead of the rest of the world

Approved SAKIGAKE-designated products

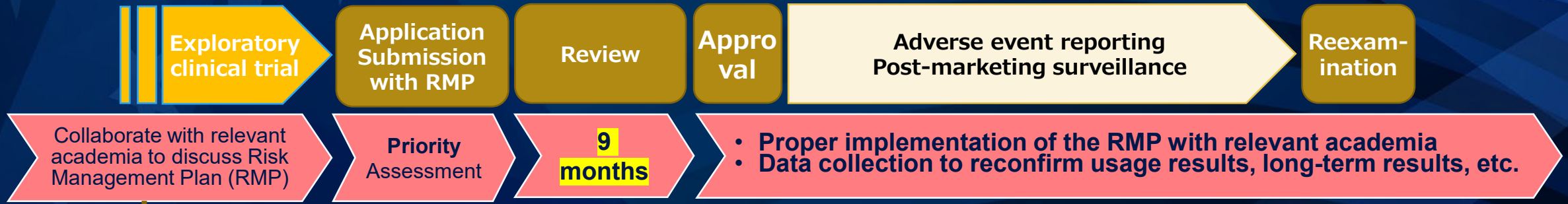
Designation Date	Name	Proposed indication	Sponsor	Approval date
2016.2.10	Titanium Bridge (Hinge-type titanium plates)	Adduction-type spasmodic dysphonia	Nobelpharma	2017.12.15
2017.2.28	Boron neutron capture therapy system (Neutron irradiation system for BNCT)	Glioblastoma, head and neck cancer (Selective destruction of tumor cells marked by boron agents)	Sumitomo Heavy Industries	2020.3.11
2017.2.28	Cancer-related gene panel examination system	Collective examination of cancer-related genes to aid decisions on cancer treatment strategies	Sysmex	2018.12.25
2018.3.27	SYNFOLIUM	Congenital cardiac disease	TEIJIN MEDICAL TECHNOLOGIES	2023.7.11

Conditional Early Approval

【Standard Review】



2017~ 【Conditional Early Approval】



【Designation Requirements for Conditional Early Approval】

1. For serious diseases for which there is no effective treatment
2. Certain clinical data are available for evaluation, but it is considered difficult to conduct a new clinical trial.
3. Can develop appropriate use criteria in collaboration with relevant academic societies and present Risk Management Plan (RMP) for post-marketing data collection and evaluation.

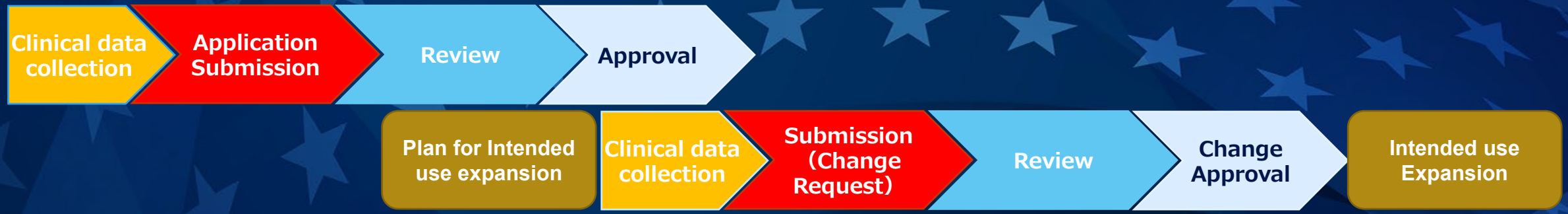
Example for Conditional Early Approval

Name	Indication	Sponsor	Approval date
SAPIEN 3	TAVI* for the treatment of right ventricular outflow tract epicardial conduit or pulmonary valve insufficiency in the pulmonary valve position implanted in congenital heart disease surgery with high surgical risk * Transcatheter Aortic Valve Implantation	Edwards Lifesciences	2020.9.11

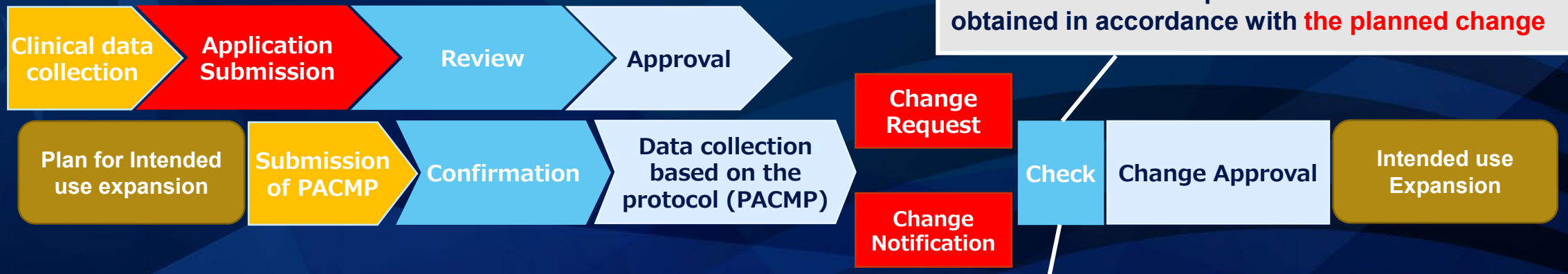
PACMP（Post-Approval Change Management Protocol）

PACMP is introduced for medical devices to enable continuous improvements through product lifecycle.

【Standard Review for Intended use expansion】



【Review using PACMP for Intended use expansion】



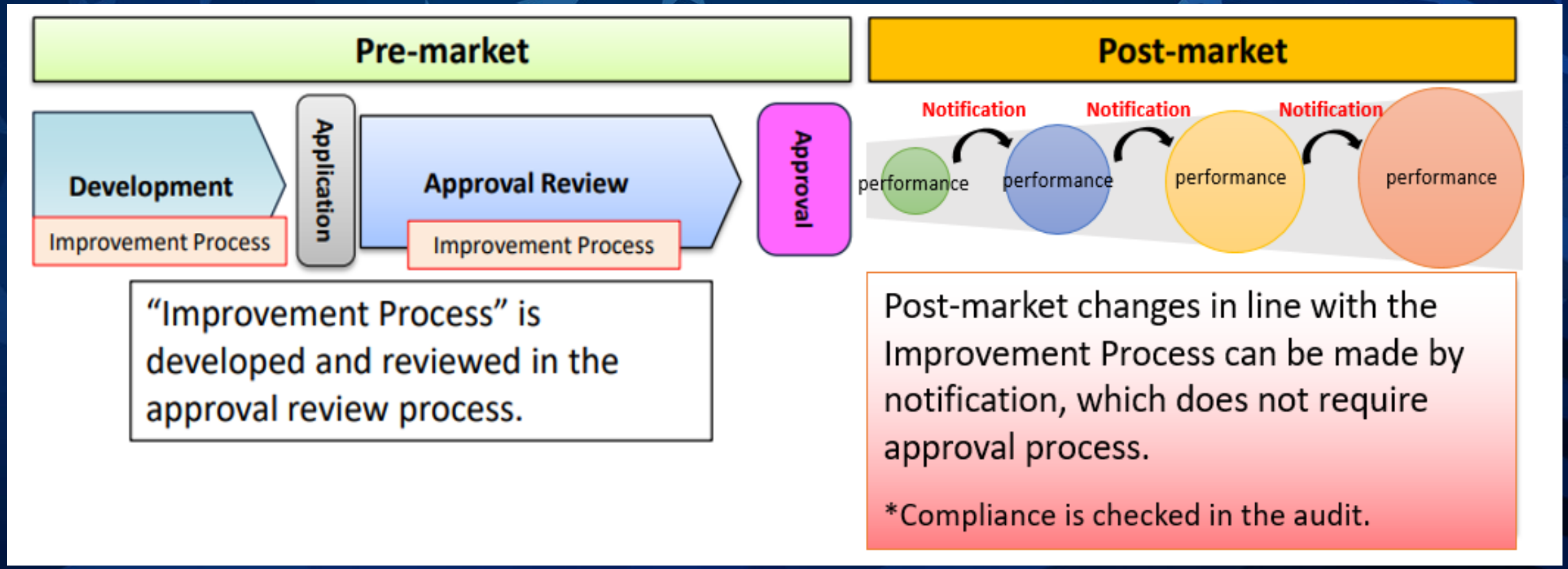
Check to ensure the predetermined results are obtained in accordance with the planned change

Objects for submission

- Change of sizes, components, performances, etc.
- Improvement of diagnostic accuracy by using post-marketing RWD

Conceptual Sketch of PACMP Using AI Technologies

- Approval review process which enables continuous improvement of performance of SaMD using AI
- Changes of performance must be in one-direction (improvement) and be managed by MAH.
- MAH may develop a process which ensures such performance changes as improvement process and submit it in the approval review process.



Approvals of medical devices are withdrawn in the case that a change is out of the approved improvement process and performance does not improve as approved improvement process.

Medical Device Approval Review Using Real World Data

MHLW develops regulatory systems supporting pragmatic trials using registries (electronic health records).

- **Edwards SAPIEN 3**

(Additional application of TAV in TAV)
Instead of conducting a new clinical trial, using the STS/ACC TVT Registry data

- **SATAKE Hot Balloon Catheter**

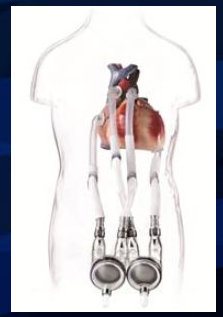
(Paroxysmal atrial defibrillation therapy for high-frequency ablation catheters)
Comparison with results using conventional methods from the Japanese Catheter Ablation Registry of Atrial Fibrillation (J-CARAF) of Japanese Heart Rhythm Society (JHRS).

- **Kawasumi Najuta Chest Stent Graft System**

(Stent graft for prevention of aortic aneurysm rupture)
Comparison with results from surgery from the historical control group of Japan Adult Cardiovascular Surgery Database（JACVSD）

- **EXCOR Ventricular assist system**

Comparison with the matching patient group survival rate from the ECMO treatment registry: Extracorporeal Life support Organization



Publication of Points to Consider for SaMD

Technical review points for some specific SaMD

- Treatment planning program for peritoneal dialysis
- Treatment planning support program for dental implant
- Treatment planning program for eye surgery
- Supporting software for detecting lesion with endoscopic imaging
- Computer diagnostic support program aimed at supporting interpretation of medical images

Discussion report of PMDA Science Board on AI-based SaMD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