

# Effort on the infrastructure of Real World Data Collection in Japan - Japanese Regulatory View -

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# Meanings of Post-Marketing Surveillance (Use-Results Survey, Re-examination)

- As the number of patients and the evaluation period are limited in pre-market clinical trials, unknown adverse events might be found after the device is introduced into the market.
- While a device is used at limited medical institutions in a clinical trial, the device will be extensively used in actual clinical practice. Therefore, the same results as those in the clinical trials may not be always obtained.



**Manufacturers are mandated to re-confirm effectiveness and safety of the device at certain point of time after approval, by collecting the actual use-results from medical institutions.**

Under the current law revised on November 25, 2014, re-examination system has been transformed into use-results survey system.

- **Re-examination System (under the previous law)**

1. Re-examination was mandated for brand-new medical devices.
2. Re-examination period was uniformed across the category\*.

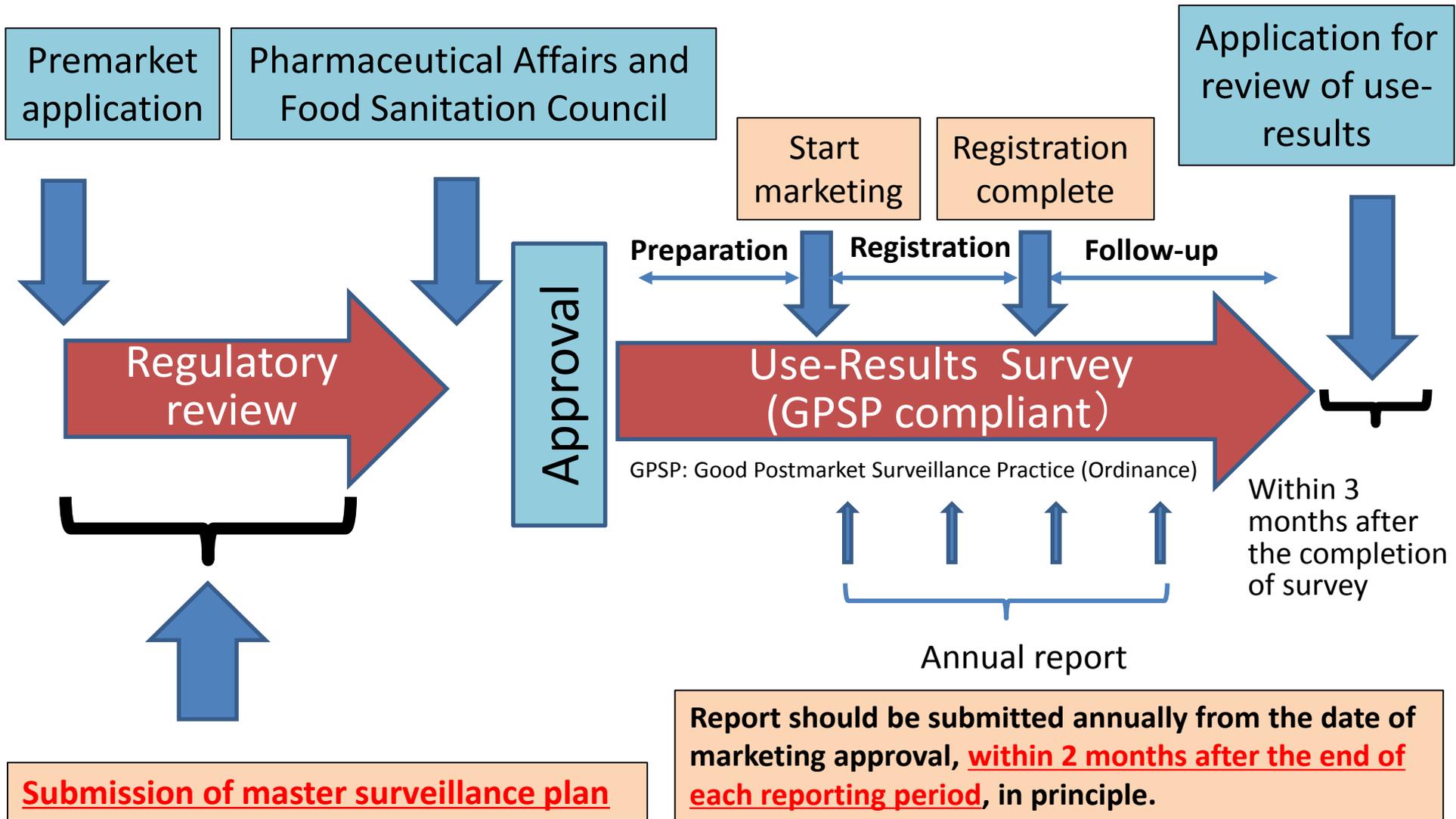
\*Category : Orphan MD : 7 years, MD with novel structure: 4 years, Other MD: 3 years

- **Use-Results Survey System (under the current law)**

1. Use-results survey, for the time period as necessary, is obligated for the devices for which survey is required\*.
2. Applicants may reasonably decide the evaluation period on their own judgments, as the system allows some flexibility.

\* Devices requiring survey: Mainly brand-new medical devices, that have no similar devices in or outside Japan.

# Overall Process of Use-Results Survey



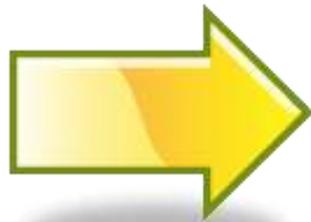
# Post-marketing registry incorporating Use-Results Survey with academic society

- While social needs for implantable VAD was very high, the associated risks were also expected to be high.
- In Japan, conducting a large scale clinical trial was virtually difficult.
- However, in the actual clinical settings in Japan, the duration of implantation was fairly long.
- Further development and improvement were desired in this area.

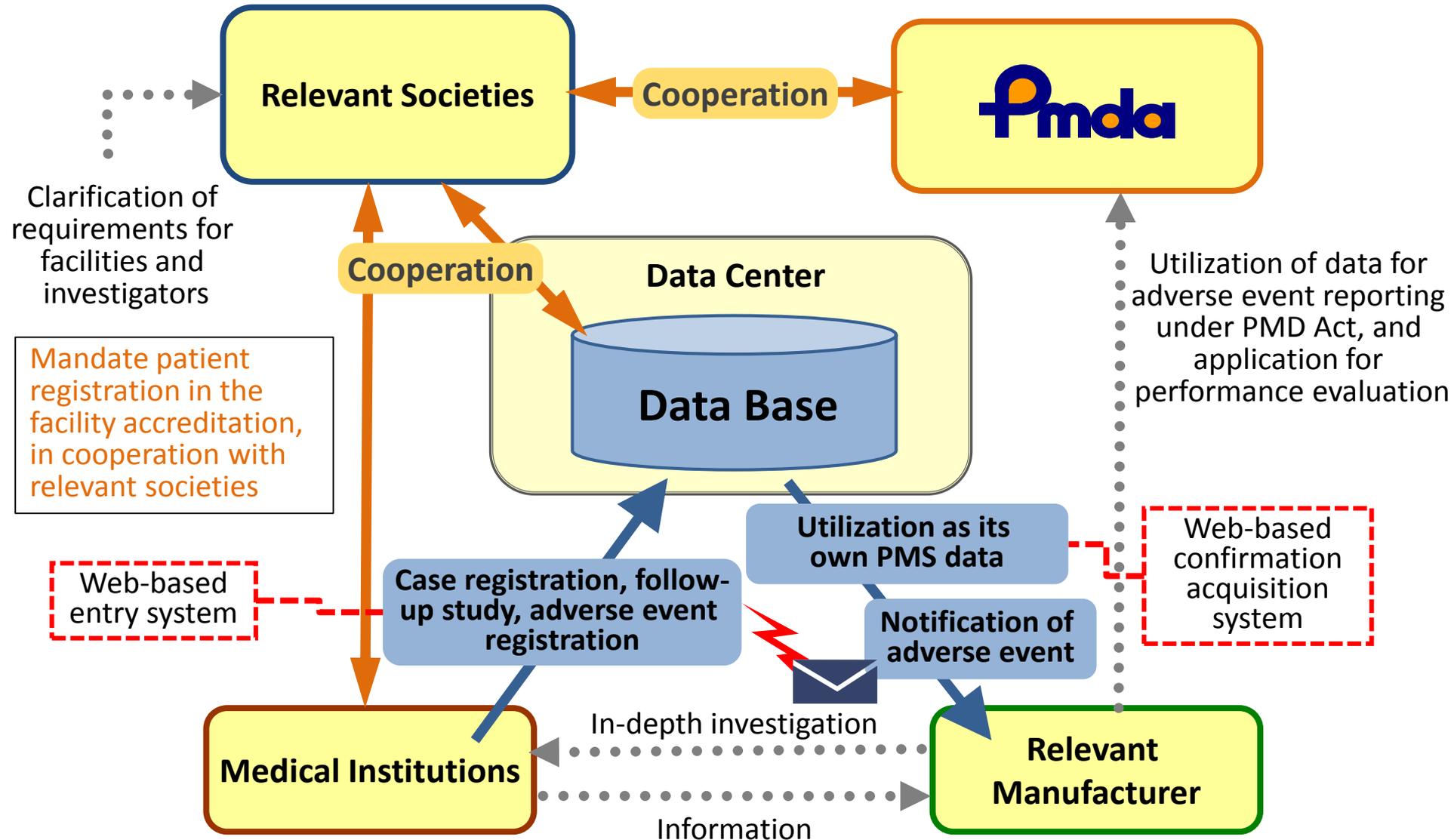
In order to facilitate early approvals of VADs under these circumstances;

It is necessary to establish a system, where minimal data is collected up for each approval, then longer-term data is continually collected in the post-market settings.

These devices are presently targeted as the subject of post-market registries.



# Schematics of J-MACS



# Recent Real World Evidence in Japan with Use-Results Survey or Re-Examination

- **Implantable VAD**

Japanese registry for Mechanically Assisted Circulatory Support: First Report.

Nakatani et al. J Heart Lung Transplant. 2017.

- **Zilver PTX**

Zilver PTX Post-Market Surveillance Study of Paclitaxel-Eluting Stents for Treating Femoropopliteal Artery Disease in Japan: 12-Month Results.

Yokoi H et al. JACC Cardiovasc interv 2016.

 **This evidence was used for partial change application to FDA**

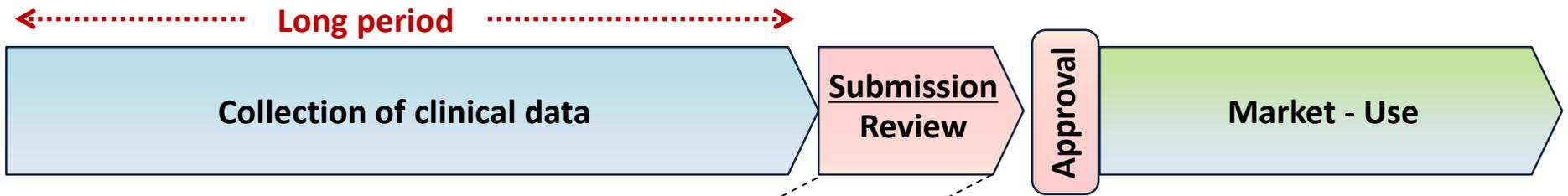
# Early Approval for Innovative Medical Devices (Fast-Break Scheme)

## Background

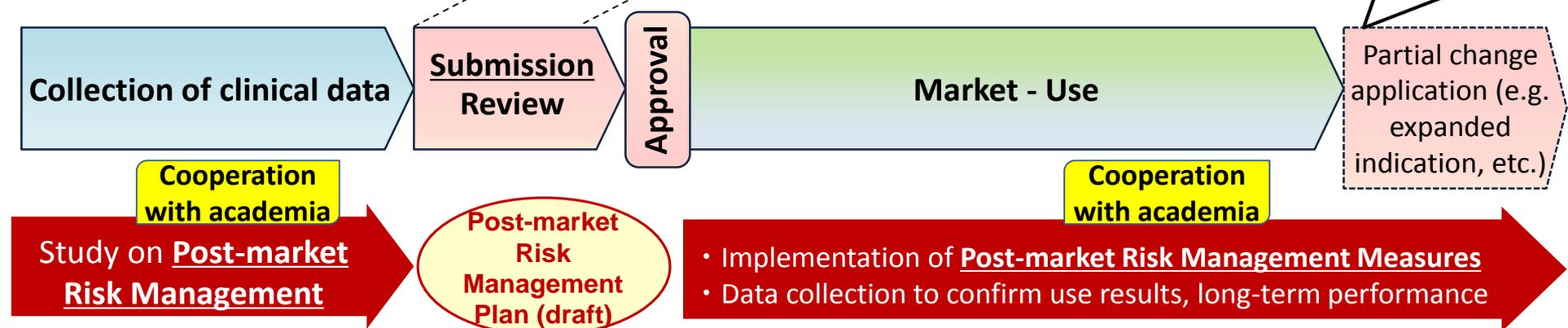
- In some cases, development may be prolonged and the patients' access to novel devices will be delayed, where considerable time period is required for gathering sufficient cases of clinical trials, in order to solidify the evidences.
- In particular, where the diseases are life-threatening and no established effective therapy is known, measures for enabling earliest possible access to the medical devices that can potentially treat such diseases, while ensuring the safety and the effectiveness, are much needed.

# Concept of Fast-Break Scheme

## Traditional approval process



## Fast-Break Scheme



Early approval will be given, without an additional clinical trial, contingent upon Post-market Risk Management.

# Fast-Break Scheme Criteria

- No appropriate alternative medical devices, or a reasonable likelihood of higher efficacy and safety compared to existing products.
- Life-threatening disease or significant disability in a daily life.
- Some supporting clinical evidence is available.
- Post-marketing commitment to an appropriate risk management plan and rigorous real-world evidence collection and evaluation.
- Justification of difficulty to conduct a new prospective clinical trial.

# Conclusions

- In Japan, the infrastructure for real world data collection has been moving forward.
- On July 31, 2017, MHLW enacted “fast-break scheme” for innovative medical devices.
- In this scheme, rigorous post marketing data collection will be especially important for risk management and innovative medical device development.
- This new framework is expected to provide greater benefits to patients who require new medical devices and to companies via improved transparency and predictability.