CRT23 CARDIOVASCULAR RESEARCH TECHNOLOGIES

"Harmonization by Doing: US-Japan Synergies in Regulatory and Clinical Approaches"
Practice Approaches to Applying Real-World Clinical Evidence

Framework for RWE use in Japan:

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I have no relevant financial relationships

Agenda

1. Examples of real-world evidence (RWE) in regulatory decision making of medical devices

2. Trends and regulatory supports to use RWE more sufficiently

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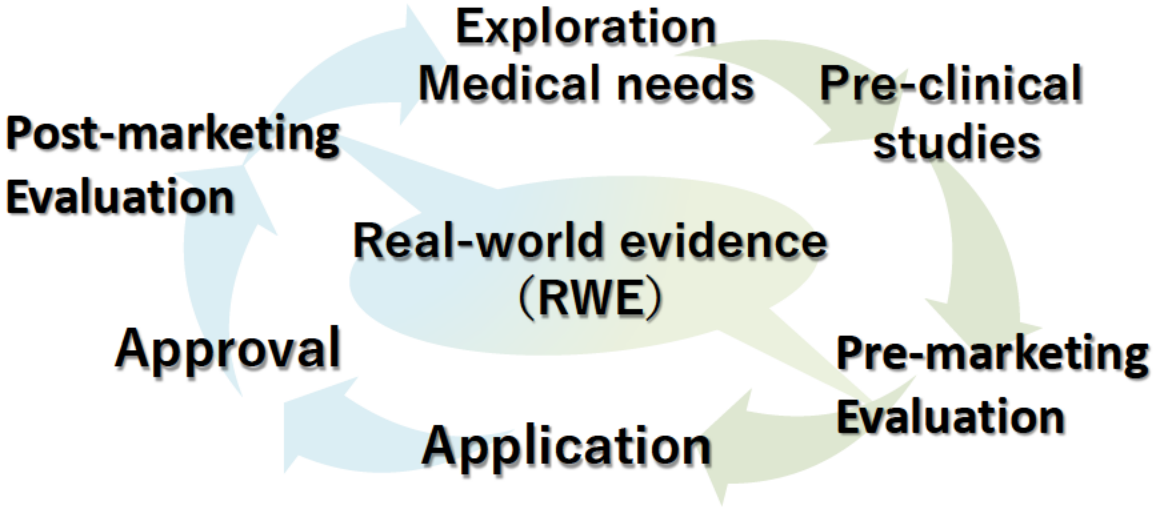
1. **Examples of real-world evidence (RWE) in regulatory decision making of medical devices**

2. **Trends and regulatory supports to use RWE more sufficiently**

The importance of RWE in clinical evaluation through device lifecycle

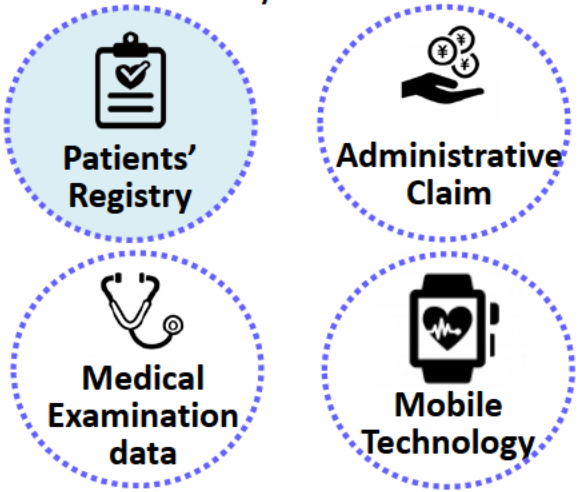


Utilization of RWE through pre- and post-marketing phase is often effective for development of medical devices required repeated improvements and medical devices for orphan disease.

RWE Utilization to Evaluate Clinical Outcomes of Medical Devices

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

Case Examples of RWE Utilization

■ Kawasumi Najuta Thoracic Stent Graft System [1]
(Kawasumi Laboratories, Incorporated , Approved in 2012)

- Aortic stent graft
- Comparison with patients registered in the Japan Adult Cardiovascular Surgery Database (JACVSD)

■ MitraClip NT system [2]
(Abbott Medical Japan LLC, Approved in 2017)

- Percutaneous repair system for mitral valve coaptation failure
- Comparison with patients with medical treatment for symptomatic severe mitral regurgitation from Duke Medical Center database

[1] Review report (English translation is available); https://www.pmda.go.jp/files/000227505.pdf
[2] Review report (Japanese only) ; https://www.pmda.go.jp/medical_devices/2017/M20171128001/340733000_22900BZX00358000_A100_1.pdf

2 Primary data or complement of clinical trials

Case Examples of RWE Utilization

■ Edwards SAPIEN 3[1]
（Edwards Lifesciences Limited, Approved in 2022 ）

- Prosthetic heart valve system used for transcatheter aortic valve replacement (TAVR)
- Clinical evidence for indication expansion: Transcatheter Aortic Valve in Transcatheter Aortic (TAV in TAV)
- ✓ Transcatheter Valve Therapies (TVT) Registry

Background of pre-market review for a pre-market application in Japan

- Difficulties in conducting clinical trial

  (e.g. Patient population is limited., Target patients for TAV in TAV are elderly.)
- The reliability of TVT registry data was confirmed.
- The TAVR medical environment is similar in Japan and the US.

The first case of that registry data is used as the primary data of clinical evaluation in Japan.

DAY1 10:50 – 11:00 AM Use of Foreign RWE in Japan – Case Study
Chie Iwaishi (Edwards Lifesciences Limited)

[1] Review report (Japanese only)https://www.pmda.go.jp/medical_devices/2022/M20221018001/170492000_22800BZX00094_A100_2.pdf

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Case Examples of RWE Utilization

Brand-new Drug/Device → Development → Approval → Post-marketing → Post-marketing Evaluation

Data entry

Institutions

JSNET*

Data provision

Contract

Industry

PMS application using the database

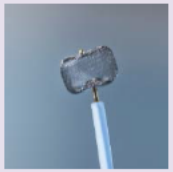
PMS application

Regulator

Device-specific registry

PulseRider
(Johnson & Johnson K.K.)

Woven EndoBridge Device
(Terumo Corporation)



JSNET 特定非営利活動法人 日本脳神経血管内治療学会

* The Japanese Society for NeuroEndvascular Therpy

Agenda

1. Examples of real-world evidence (RWE) in regulatory decision making of medical devices

2. **Trends and regulatory supports to use RWE more sufficiently**

Trends of RWE Utilization in Japan

2016 Clinical Innovation Network (CIN)* was constructed as a infrastructure for registry utilization

*The Japanese framework for accelerating use of RWE in development of medical products

2019 A new consultation category about reliability of the registry data for the application to PMDA was launched.

2021 Guidance for the utilization and reliability of registry was published.[1]

- Basic principles on Utilization of Registry for Applications

PSEHB/PED Notification No.0323-1, PSEHB/MDED Notification No.0323-1, March 23, 2021

- Points to Consider for Ensuring the Reliability in Utilization of Registry Data for Applications

PSEHB/PED Notification No.0323-2, PSEHB/MDED Notification No.0323-2, March 23, 2021

[1] https://www.pmda.go.jp/english/rs-sb-std/rs/0023.html

Basic principles on Utilization of Registry for pre-market Applications

It shows the principles for applicants utilizing registry data to explain the efficacy and/or safety in documents of clinical data for the applications.

General points to consider

- ✓ Protection of personal information
- ✓ Reliability of registry data utilized
- ✓ Appropriateness of registry data utilized
- ✓ Discussion with registry holder

- ✓ Patient population
- ✓ Endpoints
- ✓ Evaluation period
- ✓ Statistical method

PSEHB/PED Notification No.0323-1, PSEHB/MDED Notification No.0323-1, March 23, 2021

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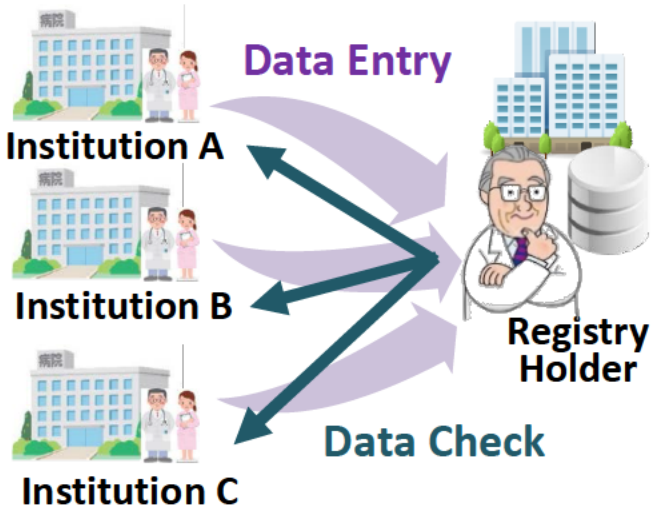
Points to Consider for Ensuring the Reliability in Utilization of Registry Data for Applications

It shows the points to consider for applicants' ensuring the reliability in utilization of data from the registries as a clinical data in the data/documents for the applications.



1. **Governance by registry holders**
   - ☑Establishment of operation and management system
   - ☑Policy on securing transparency and access to registry data
2. **Computerized system**
   - ☑Quality management of the computerized system
   - ☑Security of computerized system
3. **Quality Management of registry data**
   - ☑Data collection methods ☑Handling of collected registry data ☑Monitoring ☑Data migration from hospital information system to a computerized system
4. **Quality Assurance for Registry**
5. **Data Extraction and Datasets Preparation**

PSEHB/PED Notification No.0323-2, PSEHB/MDED Notification No.0323-2, March 23, 2021

Consultations for Development and Utilization of Registry

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

Number of cases (FY2019~FY2021)

	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	4
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

Utilization of RWD for Insurance Reimbursement of Medical Devices

1. Utilization for "Challenge Application"

Target medical devices

- ✓ Long-term implantable medical devices
- ✓ Medical devices involving innovative technologies

Clinical data collection → Application → Review (PMDA) → Approval ★ → Post Marketing Evaluation ★

★ Insurance Reimbursement Application

Expected to extend device life with increased battery capacity

2. Utilization for PACMP (Post-Approval Change Management Protocol)

Target medical devices

- ✓ AI medical devices

Clinical data collection → Application → Review (PMDA) → Approval ★

Plan for application expansion → Submission of **PACMP** → Confirm → Data collection based on the protocol → Change request → Check (PMDA) → Change Approval ★ → Application expansion

Revisions to the payment system

Conclusion

◆ **The collaboration between academia, industry and regulator is important to accelerate the utilization of RWE.**

Institutions
- ✓ Having staff for entering data
- ✓ Keeping doctor's motivation for establishing RWE

Regulators
- ✓ Building infrastructure for sustainable RWD collection
- ✓ Accompanied consultation

To collect valuable RWD for US/Japan
- ✓ Endpoints
- ✓ Evaluation period
- ✓ Reliability of data
- ✓ Cost-saving

Data Holders
- ✓ Appropriate endpoints and evaluation period
- ✓ Securing human resources and robust system to ensure data quality

Industries
- ✓ Making efficient use of RWD
- ✓ Sponsorship

◆ **We need to continue discussing for more sufficient RWE utilization.**

11:00-11:50 Panel Discussion
– What specific steps can be taken to facilitate use of RWE across countries?


Thank you for your kind attention.
If you have any questions, please contact us.
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