The outlook for Patient Involvement in Medical Device Development ~Japanese Regulatory View~

Takeshi Shiba, Ph.D.

Reviewer

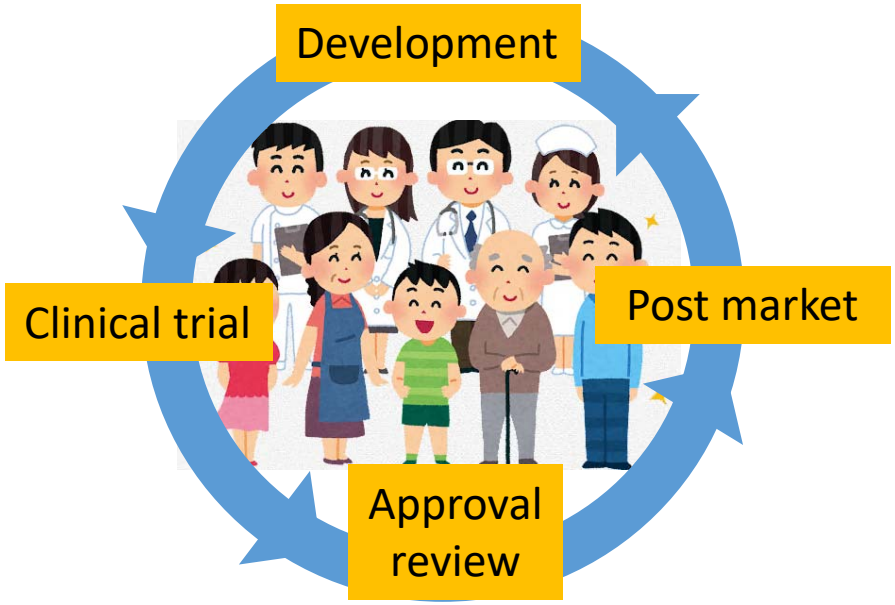
Office of Medical Devices Ⅰ,PMDA

Today‘s Agenda

1. Patient Centricity Working Group within PMDA
2. Patient-reported outcomes (PROs)
3. Mobile Health and clinical trials

Patient involvement in the medical product life cycle

In recent years, efforts like patient-focused medial products development, approval review and safety measures have become internationally significant.



In Japan

Japan Pharmaceutical Manufactures Association

“A guidebook for pharmaceutical companies to carry out activities based on Patient Centricity-Drug development that utilizes the voice of patients-” （September 2019）

“Drug development that utilizes the voices of patients Communication guidebook for pharmaceutical companies to promote activities based on patient groups and Patient Centricity” （September 2019）

Japan Agency for Medical Research and Development(AMED)

“Patient and Public Involvement (PPI) Guidebook-As the first step toward collaboration between patients and researchers-” （March 2019）

Patient Centricity Working Group within PMDA

- **Purpose**

  regarding drugs and medical devices development and safety measures

  ✓**to share the challenges from the patient‘s perspective and communicate with patients**

- **Launched** May 2019

- **Goals**

  PMDA is working on patient participation and collaboration :

  ✓ Optimize the way of **patient engagement**

  ✓ **Develop guidance** on the relationship between patient activities and PMDA

Guidance on Patient Participation released in 2021

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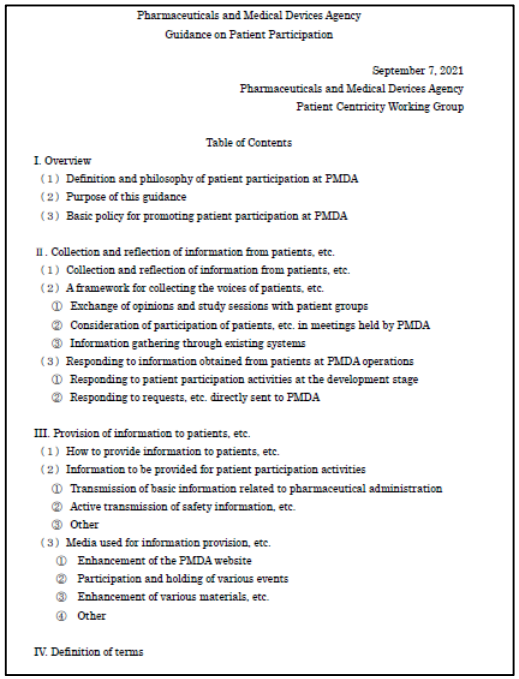
I. Overview
II. Collection and reflection of information from patients, etc.
III. Provision of information to patients, etc.
IV. Definition of terms



Pharmaceuticals and Medical Devices Agency
Guidance on Patient Participation

September 7, 2021
Pharmaceuticals and Medical Devices Agency
Patient Centricity Working Group

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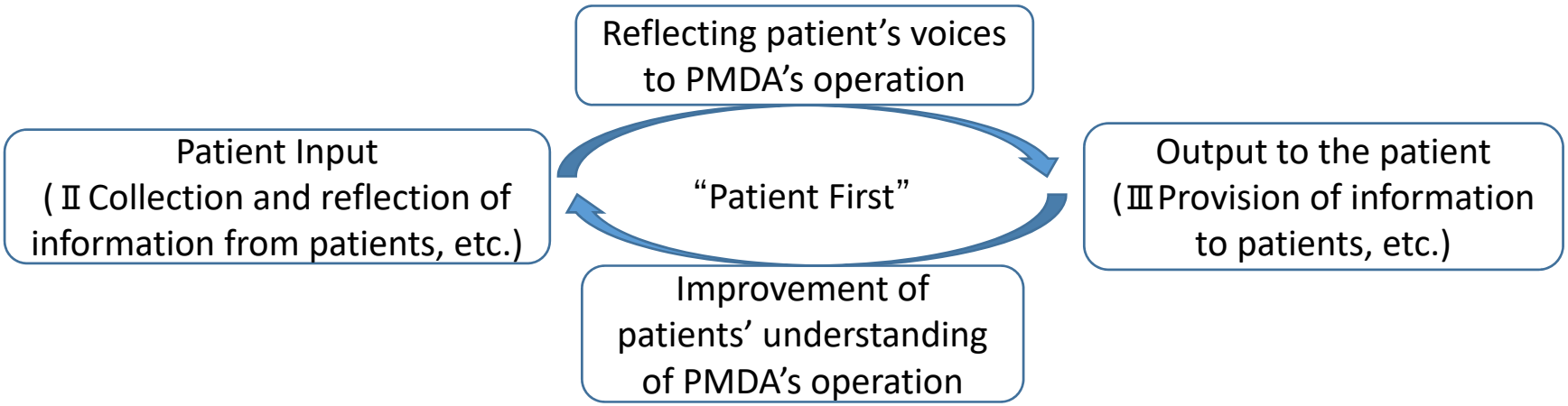
https://www.pmda.go.jp/files/000243407.pdf



Today‘s Agenda

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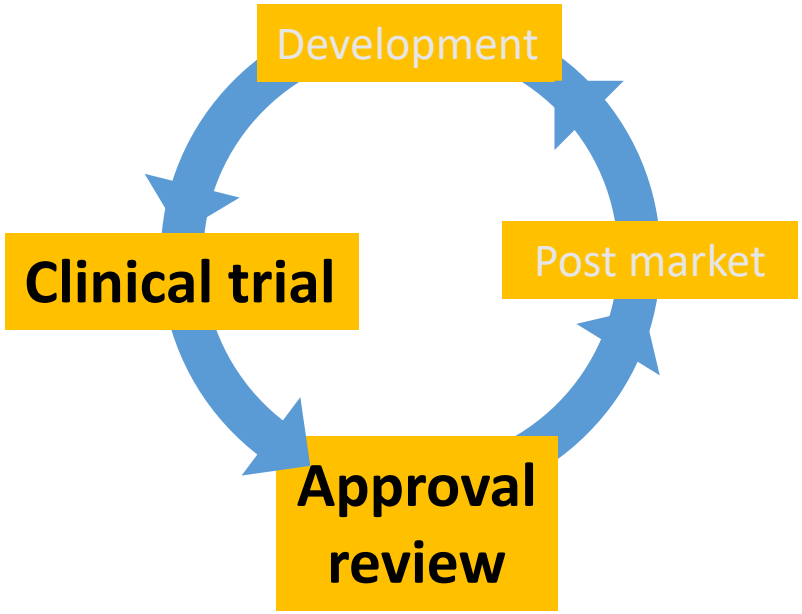


Clinical outcome assessments (COAs)

- **Patient-reported outcome (PRO) measures**
- Clinician-reported outcome (ClinRO) measures
- Observer-reported outcome (ObsRO) measures
- Performance outcome (PerfO) measures

PROs provide information on the patient's health condition as directly reported by the patient, without outside interpretation from anyone.
These outcomes are assessed using PRO instruments such as questionnaires, numeric rating scales, or diaries.

(https://www.fda.gov/about-fda/cdrh-patient-science-and-engagement-program/)

PROs example (Cardiovascular disease)

● Mitral Regurgitation

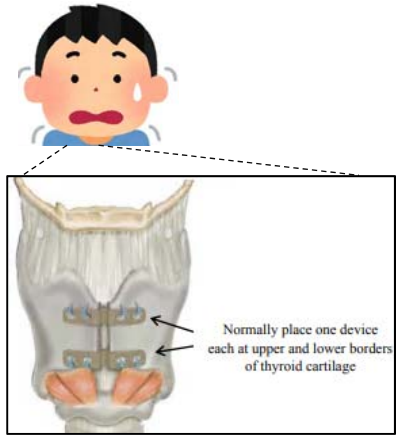
Device	MitraClip NT system (Abbott) 	
Clinical trial	**EVEREST Ⅱ High Risk Registry (US)**	**AVJ-514 trial (Japan)**
Primary Endpoint	Mortality	Major adverse events (30days) and acute procedural success
Additional Outcome measures	Echocardiography, NYHA, mortality, AE, etc **(PROs) SF-36**	Echocardiography, NYHA, 6-minutes walk test, mortality, AE, etc. **(PROs) KCCQ, SF-36**

● Aortic stenosis (low risk)

Device	SAPIEN 3 (Edwards) 	CoreValve (Medtronic) 
Clinical trial	**PARTNER 3 trial (Global)**	**Low Risk trial (Global)**
Primary Endpoint	Composite endpoint of all-cause mortality, all stroke, and rehospitalization	The rate of all-cause mortality or disabling stroke
Additional Outcome measures	Ehocardiography, NYHA, mortality, stroke, 6-minutes walk, etc. **(PROs) KCCQ, EQ-5D-5L, SF-36**	Ehocardiography, NYHA, mortality, stroke, 6-minutes walk, etc. **(PROs) KCCQ, EQ-5D**

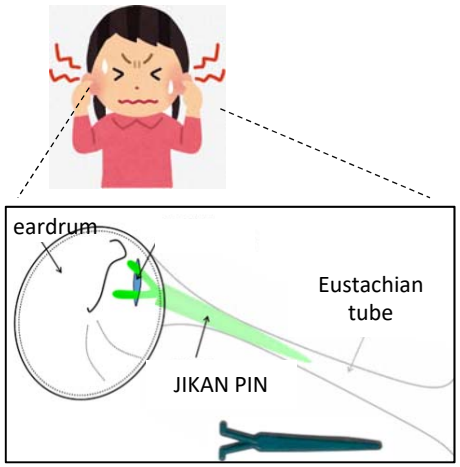
PROs example (other area)

● Adductor spasmodic dysphonia



Device	TITANBRIDGE (Nobelpharma Co., Ltd.)
Clinical trial	**Investigator initiated clinical trial (Japan)**
Primary Endpoint	The change from baseline in **VHI-10 scores (PROs)** at 13 weeks after type 2 thyroplasty with titanium bridges **VHI-10: Voice Handicap Index-10**
Additional Outcome measures	Phonatory function test, acoustic analysis assessment, etc.

● Chronic patulous eustachian tube



Device	JIKAN PIN (Fuji Systems Co., Ltd.)
Clinical trial	**Investigator initiated clinical trial (Japan)**
Primary Endpoint	The change from baseline in **PHI-10 scores (PROs)** at 3 month after surgery. **PHI-10: Patulous eustachian tube handicap inventory-10**
Additional Outcome measures	Sonotubometry, Tubo Tympano Aero dynamic graphy, etc.

PROs

■ It is important to evaluate the efficacy and safety of medical devices from the patient perspective.

✓ In cardiovascular clinical trials, questionnaires such as the SF-36, EQ-5D, and KCCQ have been evaluated as secondary endpoint. These PROs are also used in global clinical trials.

✓ PROs may be evaluated as a primary endpoint depending on the characteristics of disease/patient and the medical devices.

■ Notes on the use of PROs

✓ Clinical significance（Correlation with clinical prognosis and QOL)

✓ Reliability (Reproducibility, correlation with other objective assessments)

✓ For global clinical trials:
Validation of social background, language, etc.

Mobile Health and clinical trials

electronic PRO

✓ Improvement of input data quality (Improve input rate and access to data in a timely manner)

Wearable Device

✓ Continuous, real time data acquisition.
✓ Rapid detection of changes in the patient's condition.

- ePRO and wearable devices are expected to improve the efficiency of clinical trials and future development.

<Issues to be addressed>

✓ Due to COVID-19 pandemic, digitalization is progressing in various aspects of medical practice.
✓ In recent years, clinical trials in which subjects can participate without visiting a medical institution by utilizing online technologies such as wearable devices, ePRO, and online medical care have been attracting attention.

（Further discussion is needed on system development and actual actions.）

Summary

- PMDA has recently launched an initiative for patient engagement.

- Inclusion of PROs as an efficacy endpoint will be necessary to conduct appropriate benefit/risk assessment and to determine the true value of new medical devices.

  >For the use of a common PROs in global development

  Standardization including clinical significance and translated versions will be important.

- The idea of using digital technology to improve the efficiency of clinical trials is important. (We should proceed based on the discussion of reliability assurance and other issues.)

→Optimization of the clinical trial design to promote efficient medical device development is important!

Thank you for your attention!