PMDA’s Activities for Regulatory Utilization of Real World Data

- Introduction of New Consulting Category -

Office of Standards and Compliance for Medical Devices, Pharmaceutical and Medical Devices Agency (PMDA)

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Pharmaceuticals and Medical Devices Agency

- Established in April 2004
- Number of permanent staff
  - 256 (Apr. 2004)
  - → 936 (Apr. 2019)
- Services of PMDA
  - Review
  - Post-marketing Safety Measures
  - Relief Services for Adverse Health Effects
Three-Pillar System Unique to Japan

Comprehensive Risk Management through the Three Functions

- Consultation
- Regulatory review of drugs, medical devices
- Re-examination
- GLP/GCP/GPSP Compliance
- GMP/QMS Inspections
- Inspection of registered certification bodies
- Development of standards

Review

Reduction in risk

Safety

Continuous risk mitigation efforts

Japanese citizens

Relief

Relief measures for health damage caused by risk factors

Safety Triangle
Agenda

1. The trend of Real World Data (RWD) application
2. The application of the patient registry data
3. The system of consultation about quality/compliance of registry data
International Trend of RWD Application

International Trend
~Action to New Drug/Medical Devices Application~

- FDA: Publish the guidance
  (Use of Real-World Evidence to support regulatory decision-making for Medical devices)

- EMA: Publish the discussion paper
  (Patient Registry Initiative-Strategy and Mandate of the Cross-Committee Task Force)

- ICH GCP Renovation: Modernization of E8/ Renovation of E6

- IMDRF: Publish the guidance
  (Principles of International System of Registries linked to other data sources and tools)

Utilizing Patient Registry Data (In the Future)

- New Drugs/Medical Devices Development

- Post-Marketing Surveillance (PMS)
Japan’s Attempt of RWD Application

Clinical Innovation Network (CIN) Project

1) Clinical trial/epidemiological study design
2) Data integrity standards
3) Data set that need to be collected in each registry

- Study Group 1 (General)
  - Data integrity, Study design
  - Ethical, Application method
  - Registries retrieval system

- Study Group 2 (Establishment of New Registries)
  - Muscular dystrophy
  - Amyotrophic lateral Sclerosis
  - Orphan cancer
  - Neurosurgery

PMDA
CIN-Working Group

MHLW
Ministry of health, labor, and welfare

AMED

The Japan Agency for Medical Research and Development (AMED) is an independent administrative institution of the Japanese Government, which engages in research and development in the field of medicine, establishing and maintaining an environment for this R&D, and providing funding.
Data Integrity About Utilizing the RWD

**Use of Electronic health record data in Post-Marketing Surveillance (PMS)**

- **<Industries-PMDA collaboration>**
- **PMS**
  - **Revision of GPSP Ordinance:**
    - Publication: Oct 2017,
    - Enforcement: April 2018
  - **Notification:**
    - Points of attention about “Drug” Post-Marketing Surveillance using Big data
    - Publication: Feb 2018

**Use of Registry data in New Drugs/Medical Devices Application**

- **<AMED PMDA/MHLW>**
- **PMS**
  - **Study Group1**
  - **New Drug/Medical Devices Application**
  - **AMED Report**
    - Study Group1
  - **Preliminary Draft**
  - **Renovation of ICH E8/E6**
    - **Finalize /Publication**

*GPSP*: Good Post-marketing Study Practice
Utilization of Post-Marketing Surveillance

- The GPSP ordinance was revised to use the Big data complying the data integrity in PMS

New

Post-Marketing Surveillance using Big data

Publication: Oct 2017
Enforcement: April 2018

Notification: Points of attention about “Medical Device” Post-Marketing Surveillance using Big data (Publication Dec 2018)
The Concern About Data Integrity in the Registry Data

SCOPE

- Using as control group of clinical trial (New Drugs/Medical Devices Development)
- Using as PMS

Is our DB complying good manner and data integrity?

How we improve the quality of DB?
Map of the Registry Data of Academic Society

Organization Chart

Academic Society

Management office of the Registry Data

DB

Institution/Hospital

Roles

Management of the Society

Construction of registry DB
Data management: DM
Monitoring, Statistic, etc.

TASK

Organize the Society

Manage organization

Make SOPs

Construct the DB

Maintenance the DB

Train data handling

Make the plan

Visit the Institute

Make report

Self Check, etc.

Application for usage
The Concern About Quality/Compliance of the Registry Data

- Method of Data collection
- Method of Data management etc.

Institution A

Institution B

Institution C

Registry Data

Sponsor

- Systematic organization the Registry Data
- The method of securing the Transparency
- SOP for accessing the Registry Data from Sponsor
- The Security of the registry data etc.

Launch the new consultation system about Quality/Compliance of the Registry Data

Apr 2019
Consultation System for the Development of the Registry Data

- **Member**: Registry organization (mainly Academia Society), Sponsor (attendable)
- **Content**: Advise appropriateness of development plan utilizing registry data
  - Advise method of ensuring the data integrity of registry data for approval/reexamination applications
- **Exempt**: In case of application to the individual new Drug/Medical Device

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**Pre Meeting**
- Confirm Meeting material
  - Contents
  - Consult Schedule
- Announce the method to make consult documents
- Others

**Consultation (~ 1 hour)**
- **PLACE**: at PMDA (basically)
- **Contents**:
  - *Advice for the application plan using the Registry data*
  - *Advice for the content of the Protocols/SOPs from the perspective of ethics, data utilization, data entry, validation, etc.*

**Follow up**
- Send consultation record
- Advice the improvable points for SOPs

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Office of Standards and Compliance for Medical Device
Office of Non-clinical and Clinical Compliance

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Get it!...
Consultation System for the Quality/Compliance of the Registry Data

- **Member**: Sponsor, Registry organization (attendable)
- **Content**: Check and advice the data integrity of registry data for approval/reexamination applications corresponding to the individual new Drug/Medical Device

**Place**: at PMDA (basically)

**Contents**:
- **Check and advice the Quality/Compliance of the Registry Data according to the protocols/SOPs based on source documents**
- **In case of newly constructing the Registry Data, check and advice for the content of the Protocols/SOPs**

**Consultation**

1 Day

**Application for New Drugs/Medical Devices**
- Get the agreement about the application plan
- Fulfillment of Evaluation
- Propriety of Plan

**Usage for PMS**
- Confirm about the plan
- Fulfillment of Evaluation
- Propriety of Plan

**Pre Meeting**
- Confirm Meeting material
  - Contents
  - Consult Schedule
- Announce the method
  To make consult documents
- Others

**Follow up**
- Send consultation record
- If necessary, follow up consultation (free)
- If the critical issue about compliance and any changes is required, the additional consultation is needed (charged)
Roadmap of Guideline Development to Ensure Registry Data Integrity for Approval/Reexamination Applications

- **2019**
  - Q1: Create draft to utilize registry data for application
  - Q2: Create draft to ensure integrity of registry data
  - Q3: Develop guideline
  - Q4: Implement consultation system to utilize registry data for application

- **2020**
  - Q1: Develop guideline
  - Q2: Consultation with expert
  - Q3: Implement consultation system to utilize registry data for application
  - Q4: Check successful example!

**Working Group (WG) in CIN**

Collaborate, Share Information

AMED (Collaboration of cross-sectional research groups)
Thank You for Kind Attention

PMDA HP (English)

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