Challenge of regulatory advance for Innovation
- From Regulatory Science viewpoint -

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**Science**

**RS Microscopia**
Science for Evaluation Method (Quality, Efficacy, Safety)

**Knowledge Accumulation**

**RS Macroscopia**
Science for Evaluation Method (Comprehensive Judgment)

**Technology**

**DB**

**Technology for regulatory adaptation**

- Achievements from RS Engineering (e.g.)
  - Establish evaluation method for cutting-edge technology
  - Respond to translational research
  - Modelling & Simulation
  - Develop guidelines
  - Establish review standards
  - Draft legislation etc.
PMDA has promoted regulatory science for evaluation/judgment of quality/efficacy/safety of medical products.

Regulatory Science Center was established in April 1, 2018, centralizing PMDA’s RS-related activities to achieve followings:

- Addressing and streamlining resolution of scientific issues
- Improving quality of review and safety measures
- Activating discussions with each stakeholder by providing of RS information
Main services of the Regulatory Science Center

1. Providing services/information on cutting-edge technology
   • Collecting information on cutting-edge technology expected to be used for medical products to get ideas for evaluation and regulations through discussions with stakeholders
     ⇒ Science Board, Horizon scanning

2. Promoting use of submission data/real-world data
   • Wide use of submission data
   • Wide use of real-world data such as medical records, etc.
     ⇒ Maximize the use of submission data/real-world data for optimal use throughout product lifecycle and development of innovative products

3. Human resource development
   • Supporting staffs to deal with scientific issues and release its results
   • Promoting RS and developing human resources through partnership with academia (e.g., cross appointment program)
     ⇒ Exchange of expertise between academia and PMDA staff

Further streamlining of R&D programs and post-marketing safety measures through Regulatory Science
Regulatory Science Center
- Collaboration with other PMDA Offices -

- Offices of New Drugs
- Office of Medical Informatics and Epidemiology
- Office of Research Promotions
- Office of Advanced Evaluation with Electronic Data
- Offices of Safety
- Office of Medical Informatics and Epidemiology
- Office of Safety
- Office of Medical Informatics and Epidemiology
- Office of Research Promotions
- Office of Advanced Evaluation with Electronic Data
- Offices of New Drugs
Establish disease models
Identifying commonalities among different drugs in the same class

PMDA’s own analyzing raw data

Advices better informed by M&S, etc.

More evidences for consultation review, & guidance formulation

Modeling & Simulation: Concentration-Response
Model PBPK: Physiologically-based Pharmacokinetic Model, etc.
Analyze electronic health records, insurance claim data, diagnosis procedure combination (DPC, counterpart of US’s DRG) data, lab test results, etc.

Enables advanced pharamacoepidemiological analysis

Covers 23 major hospitals and 4 million patients (as of Feb. 2018).

Full operation since April 2018, MID-NET charges $430,000/Drug.
Science Board

Universities
Research Institutes

Medical institutions

Collaboration

Science Board

- Exchange opinions
- Between top-class researchers in Japan and PMDA reviewers
- Assess cutting-edge technologies
Subcommittee on Rare Cancers

- Consider methodologies to evaluate drugs for rare diseases, including rare cancers, with very small patient populations (no more than 50,000 patients), which makes conduct of comparative studies difficult.

Subcommittee on Drug Development

- Sort out bottlenecks for drug discoveries by academia and discuss solutions.

Subcommittee of Artificial Intelligence

- Overview new technologies using AI and discuss their totally new characteristics in order to facilitate the future review and consultations on the products.
Publication on the Journal

Regulatory Science on AI-based Medical Devices and Systems

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Abstract AI-based medical and healthcare devices 1) plasticity causing changes in system performance throughout the timing of learning and assignment of responsibilities for behavior in response to unknown inputs due to the black box nature; and 3) need of assuring the characteristics of datasets according to Artificial Intelligence and its Applications in Medical Devices Agency (PMDA), Tokyo, Japan, examined conventional technologies, thereby clarifying the characterizes the characteristics and clinical positioning of a viewpoint of regulatory science, and presents the issues related in machine learning.

Keywords: artificial intelligence, medical devices, medical


1. Introduction

The applications of artificial intelligence (AI)-based can.
Theme of Science Board (4th term)

Clinical evaluation of therapeutic agents for antimicrobial resistant infections

The review of software as a medical device utilizing computer simulation

Evaluation of diagnostic agents with new generation biomarker

The risk assessment of genome edited products
Comprehensive Partnership Agreements

Collaborative framework advanced in cooperation with academia to work with specialized medical institutions to improve medical standards in the area of RS promotion while ensuring efficacy/safety/quality and reliability

- **Partnerships** with medical schools and national advanced medical centers
- **Personnel exchange**
  Personnel exchange allows Human resources development and enhanced feasibility of cooperative activities
- **Cooperative activities**
  Details of collaborations are discussed and selected to realize efficient and unique partnership.

【Agreement with】
National Cancer Center (H28.2), Hiroshima Univ (H28.3), Keio Univ (H28.3), Tsukuba Univ (H28.3), National Center of Neurology and Psychiatry (H28.7), Tohoku Univ (H28.10), National Center for Global Health and Medicine (H29.3), National Cerebral and cardiovascular Center (H29.7), National Center for Child Health and Development (H30.1)
Research supported by AMED moving onto practical utilization is required to receive PMDA’s RS strategy/general consultations in principle.

**AMED Drug Development Support Network**

1. Planning/advising on basic/advanced research
2. Collecting/evaluating/selecting promising seeds
3. Introducing joint research organizations/study institutions
4. Supporting advanced-development research
5. Leading/collaborating/licensing out pharmaceutical companies

**PMDA RS strategy/general consultation**

1. Preparing development roadmap
2. Advising on quality
3. Advising on non-clinical study
4. Advising on clinical trials
PMDA’s support for practical use of innovation
-Consultation services for practical application of innovation advancements-

1. Overview

- A menu called “Consultation for practical application of innovation advancements” is added to the RS General Consultation to enhance advices to innovative products which do not apply existing concept. Under this “Consultation for Practical Application of Innovation Advancements”, two submenus are added: “Consultation concerning the PMD Act and Medical Insurance Issues” and “Services to provide Global Information” for innovative products. *(1) 
  - Consultations concerning the PMD Act and Medical Insurance Issues: consultation on various issues anticipated in a development phase such as handling of concomitant and companion use of products (e.g. a new drug administered based on results of a new test), combination products and program medical devices is provided.
  - Services to provide global information: regulatory information based on disclosed information of Europe and US is provided as a reference for those who are trying to expand their business to Europe and US.
- Consultation results are shared with the Venture Support Strategy Office (with applicant consent) to promote seamless advancement from product review to obtaining Japanese National Health Insurance coverage. *(2)

2. Schemes considered

- RS General Consultations
  - Provides:
    - Information on RS strategy consultation
    - Overall regulatory information on PMD Act

- RS Strategy Consultations
  - Pre-consultation meeting
    - Prepares for consultation e.g., listing topics to be discussed
  - Consultation
    - Consultation with offices of product review

(1) “Consultation for practical application of innovation advancements” will be added (in coordination with MHLW)
  - Consultation on PMD Act and medical insurance issues
  - Services to provide global information

(2) Sharing consultation results Office
  - (if agreed by the applicant)
    - further collaboration may be considered depending on its outcome
PMDA’s Horizon Scanning
-Purpose-

- Identify emerging technologies/products
- Assess their impacts on the regulation and regulatory actions (e.g. product review)
- Inform the Agency so that it can proactively address them
PMDA’s Horizon Scanning -Process-

Information Source
- Member of Science Board
- Academia
- Industries
- PMDA Staff
- Other Organizations (Research Inst., etc.)
- Foreign Organizations (FDA, EMA, etc.)

Regulatory Science Center
Identify, prioritize and analyze

Science Board

PMDA In-house Research Project

Coordination with PMDA/MHLW Offices

Science Board Reports
- Guidelines
- Suitable regulation/ evaluation etc.
PMDA’ Initiatives to Rational Medicine

1. Innovation through products approval reviews of enhanced rigor and rationality
2. Further promotion of regulatory science
3. Increased sophistication of safety measures through the use of real-world data
4. Enhanced international partnerships

PMDA makes all-out efforts for Rational Medicine!
Thank you very much!!

http://www.pmda.go.jp/en/