Challenge of regulatory advance for Innovation

- From Regulatory Science viewpoint -

3 July, 2018

3rd Japan-Korea Joint Symposium on Medical Products

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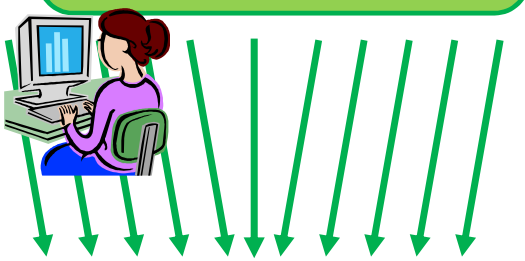
Regulatory Science

Ethical Science and Technology for the People and Society

Science → Technology

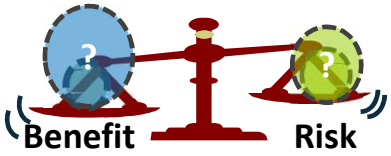
RS Microscopia
Science for Evaluation Method
(Quality, Efficacy, Safety)



DB

Knowledge Accumulation

RS Macroscopia
Science for Evaluation Method
(Comprehensive Judgment)



DB

Knowledge Accumulation

Deduction

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.**

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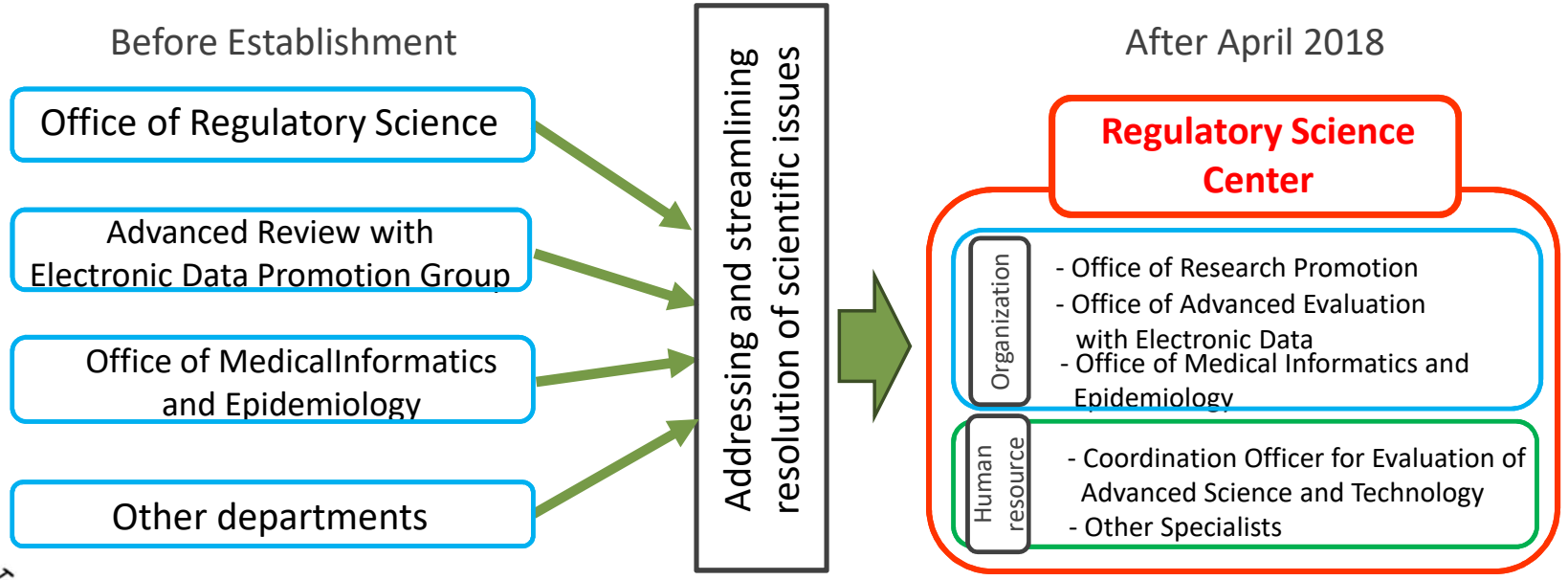
Establishment of the Regulatory Science Center

- PMDA has promoted regulatory science for evaluation/judgment of quality/efficacy/safety of medical products
- Regulatory Science Center was established in April1, 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



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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

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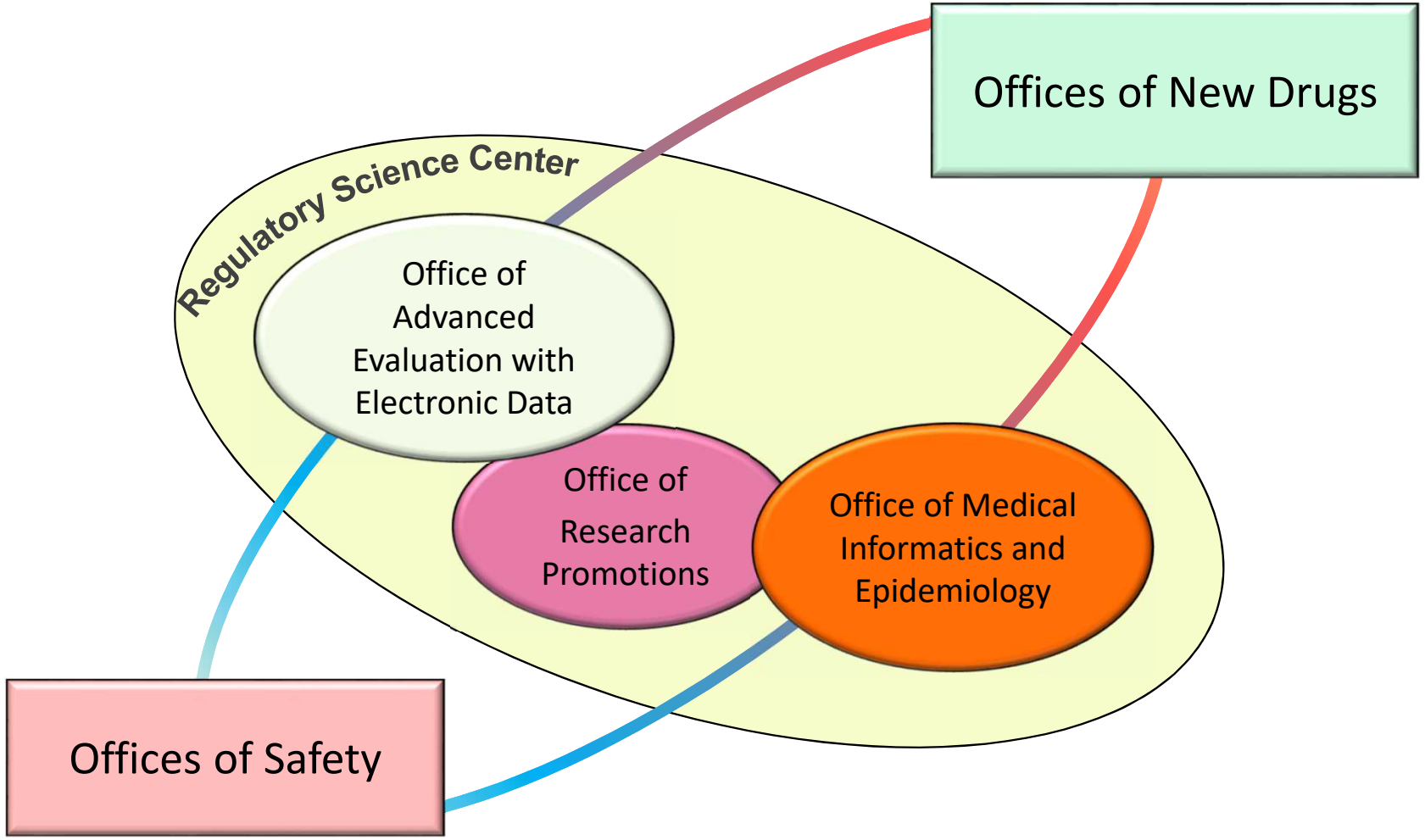
Regulatory Science Center
- Collaboration with other PMDA Offices -



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Analysis of CDISC Data Submitted with New Drug Application

[NDA]

CDISC Data

Database of Clinical Trial Results

Analysis

M&S, MPBPK

NDA Review → Advanced review

- PMDA's own analyzing raw data

Scientific Consultation → Improved development

- Advices better informed by M&S, etc.

Cross-Products Analysis → More evidences for consultation review, & guidance formulation

- Establish disease models
- Identifying commonalities among different drugs in the same class

Modeling & Simulation: Concentration-Response
Model PBPK: Physiologically-based Pharmacokinetic Model, etc.

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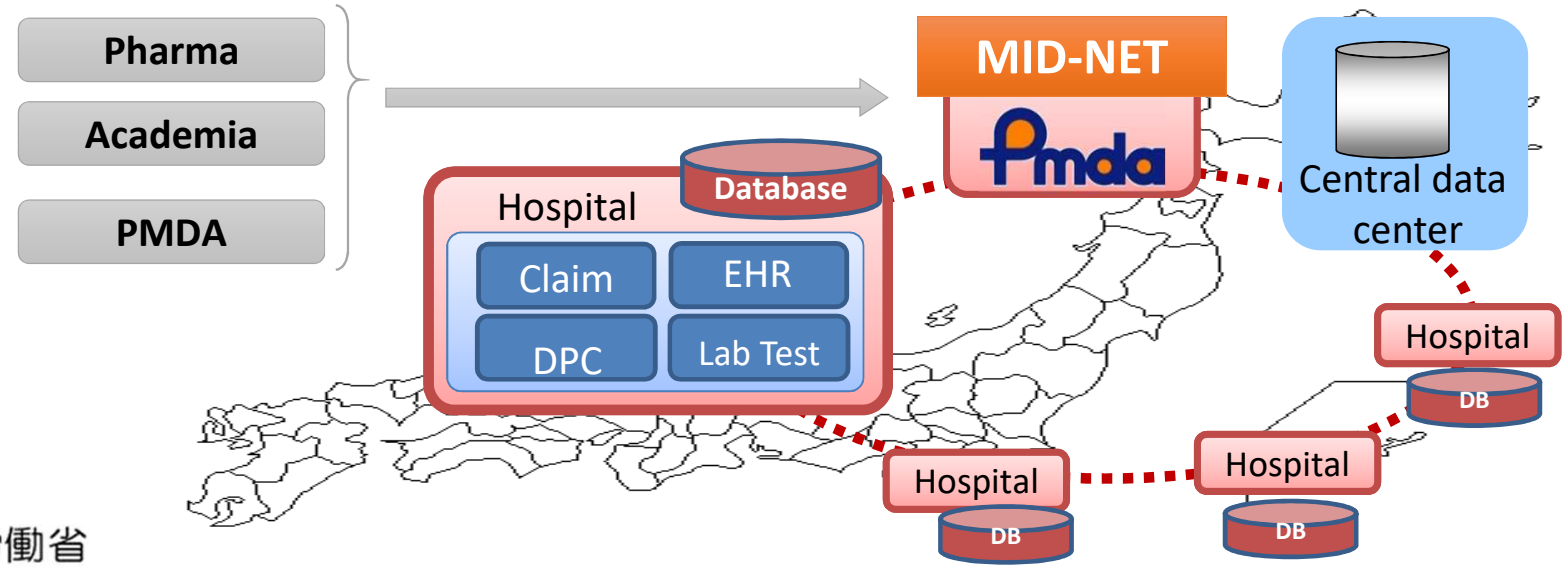
MID-NET® (Medical Information Database Network) Project

- 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.



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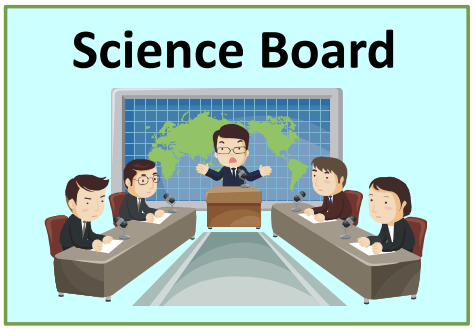
Science Board

Universities
Research Institutes

Medical institutions

Collaboration



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

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Reports of Science Board (3rd term (FY2016 – 2017))

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

Advanced Biomedical Engineering
7: 118–123, 2018.

Invited Review Paper

DOI:10.14326/abe.7.118

Regulatory Science on AI-based Medical Devices and Systems

Kiyoyuki Chinzei,[1] Akinobu Shimizu,[2] Kensaku Mori,[3] Kanako Harada,[4] Hideaki Takeda,[5]
Makoto Hashizume,[6] Mayumi Ishizuka,[7] Nobumasa Kato,[8] Ryuzo Kawamori,[9] Shunei Kyo,[10]
Kyosuke Nagata,[11] Takashi Yamane,[12] Ichiro Sakuma,[4] Kazuhiko Ohe,[13] Mamoru Mitsuishi[14,#]

Abstract AI-based medical and healthcare devices
1) plasticity causing changes in system performance throu
the timing of learning and assignment of responsibilities fo
havior in response to unknown inputs due to the black bo
tion; and 3) need of assuring the characteristics of datasets
mittee on Artificial Intelligence and its Applications in Me
and Medical Devices Agency (PMDA), Tokyo, Japan, exa
conventional technologies, thereby clarifying the character
summarizes the characteristics and clinical positioning of
viewpoint of regulatory science, and presents the issues re
in machine learning.

Keywords: artificial intelligence, medical devices, medica

Adv Biomed Eng. 7: pp. 118–123, 2018.

1. Introduction

The applications of artificial intelligence (AI)-based new

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DOI: 10.1111/cas.13568

REPORT

WILEY Cancer Science

Current state of therapeutic development for rare cancers in Japan, and proposals for improvement

Akira Kawai[1,2] | Toshio Goto[1,3] | Tatsuhiro Shibata[1,4] | Kenzaburo Tani[1,5] |
Shuki Mizutani[1,6] | Akiyoshi Nishikawa[1,7] | Taro Shibata[1,8] | Seiichi Matsumoto[1,9] |
Kyosuke Nagata[1,10] | Mamoru Narukawa[1,11] | Shigeyuki Matsui[1,12] |
Masashi Ando[1,13] | Junya Toguchida[1,14] | Morito Monden[1,15] | Toshio Heike[1,16] |
Shinya Kimura[1,17] | Ryuzo Ueda[1,18]

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[3]Program for Drug Discovery and Medical Technology Platforms, RIKEN, Tsukuba, Japan

Theme of Science Board (4th term)

Clinical evaluation of therapeutic agents for antimicrobial resistant infections

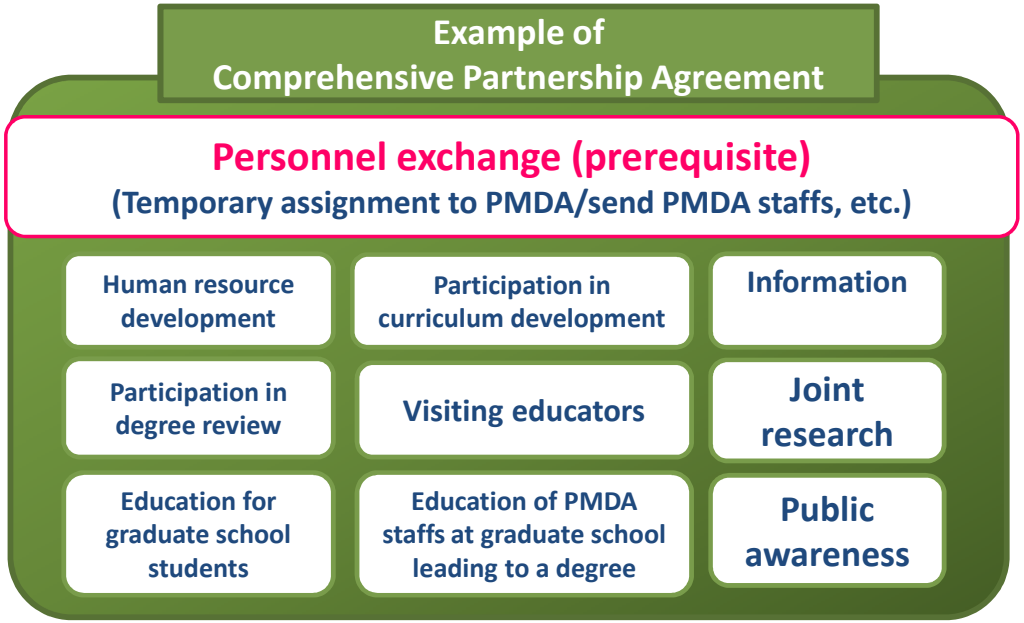
The review of software as a medical device utilizing computer simulation

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)

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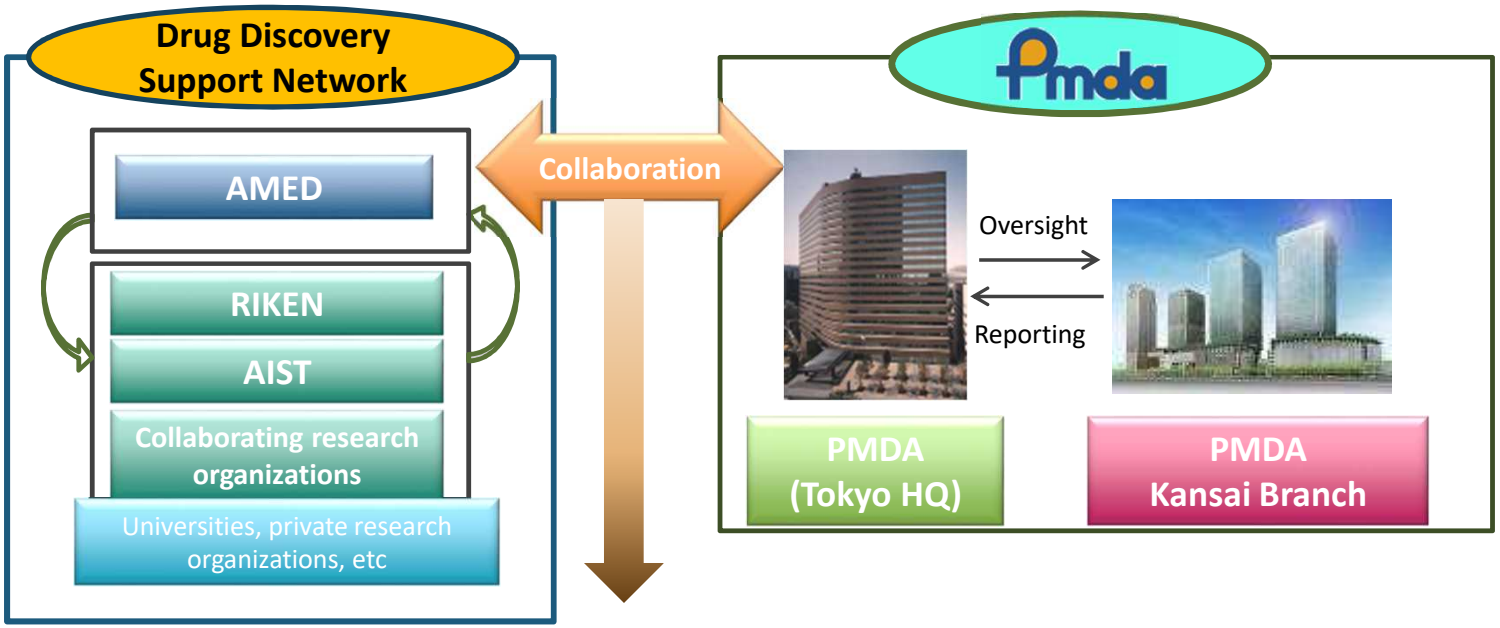
Collaboration with Drug Discovery Support Network



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

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PMDA's support for practical use of innovation
-Consultation services for practical application of innovation advancements-

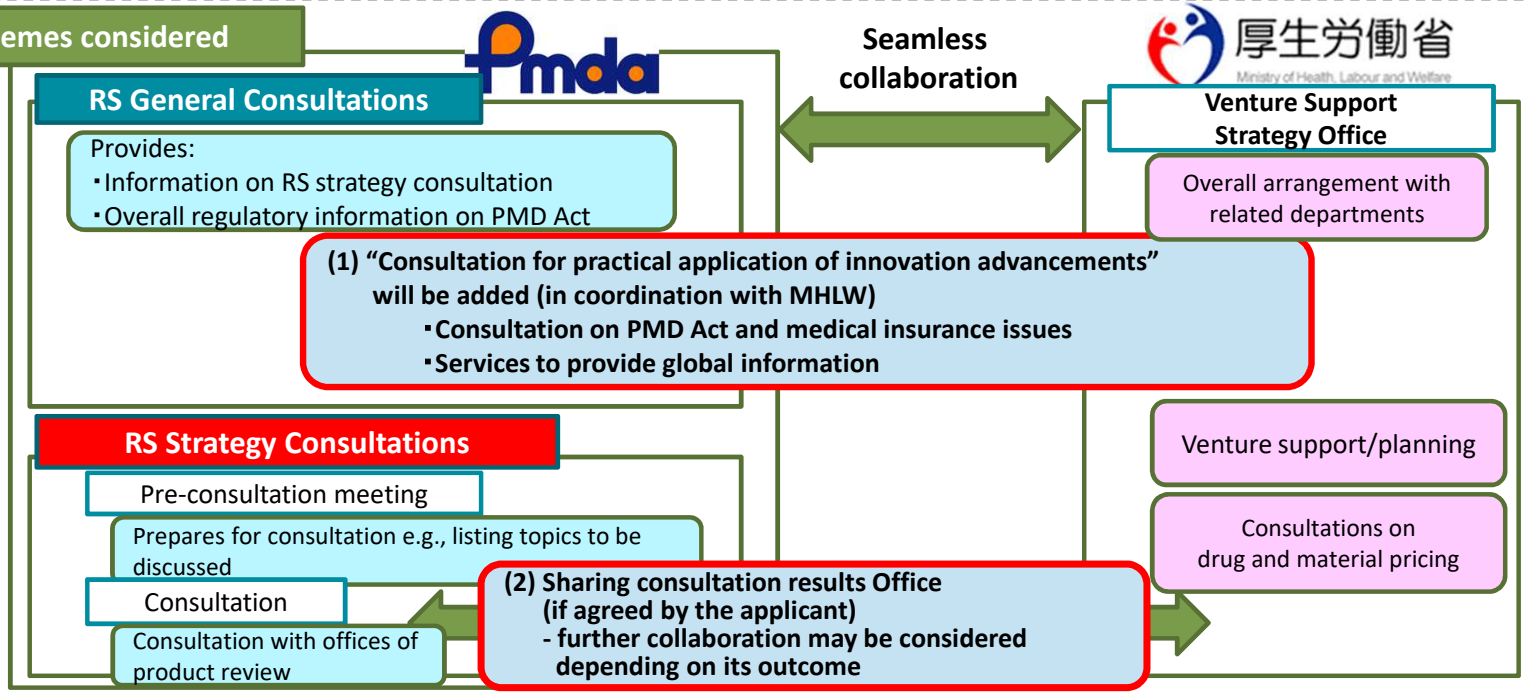
1. Overview

○ 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



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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

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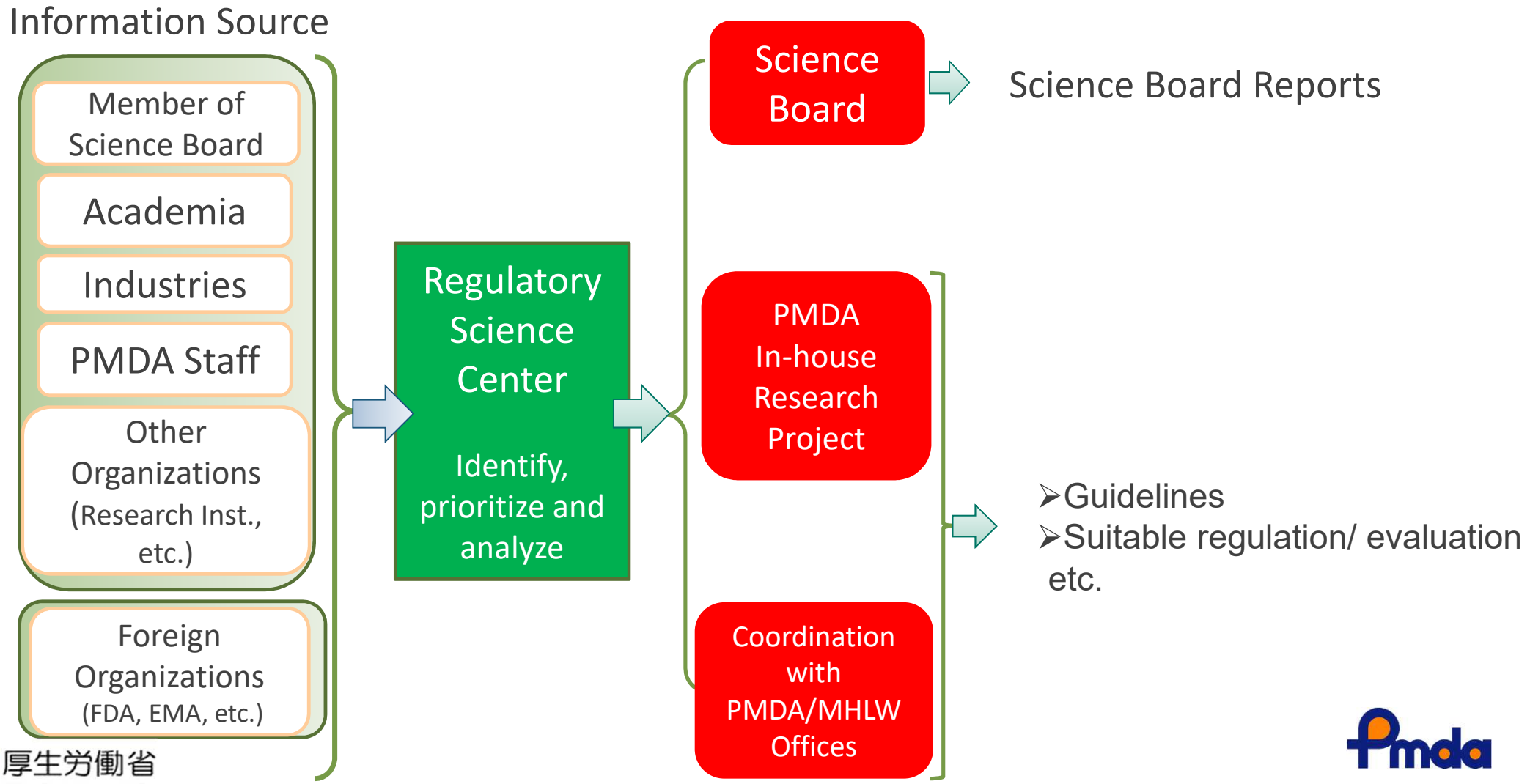
PMDA's Horizon Scanning -Process-



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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!

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Thank you very much!!

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

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