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The Future of PMDA

Yasuhiro Fujiwara, M.D., Ph.D.
Chief Executive, PMDA

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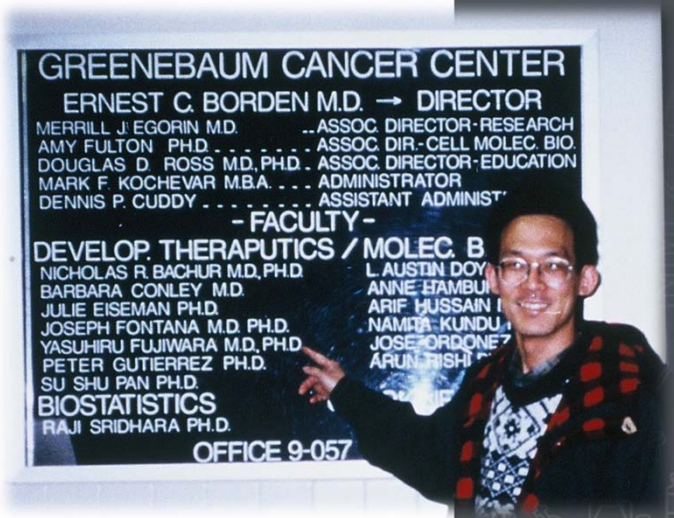
Yasuhiro Fujiwara, M.D., Ph.D.

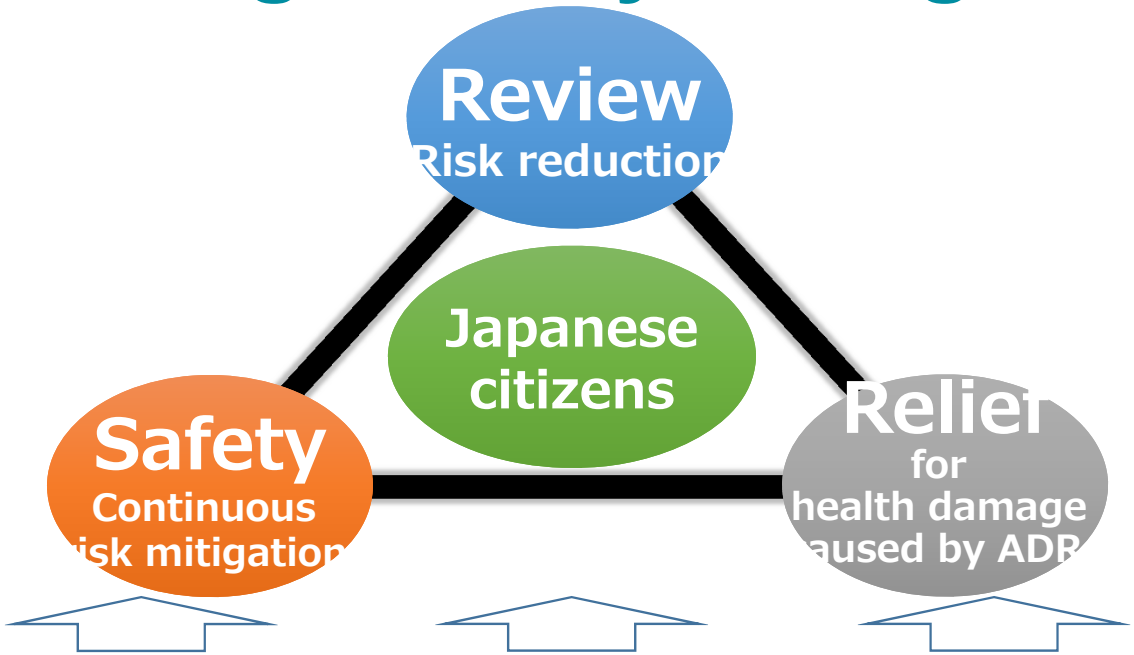
- **Chief Executive of PMDA** (since 2019.04)
- Deputy Director of the Hospital (Research), National Cancer Center Hospital (since 2015.04)
- Director-General, Strategic Planning Bureau of the National Cancer Center (since 2012.07)



Experience:

- ***Medical Oncologist**, specializing in breast cancer*
- *Oncology drug **reviewer** (1997-2002)*

Comprehensive Risk Management through Safety Triangle



- Improving quality of services by promoting regulatory science
- Promoting globalization
- Developing the governance/compliance system based on organizational role and social position

As the only regulatory authority in the world to play these 3 roles in an integrated manner, PMDA contributes to improvement of the standard of medical care by delivering safer and higher quality products faster to medical practice, and plays an active role to prolong people's healthy life expectancy based on regulatory science

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4th Mid-Term Plan (FY2019-2023)

1． Active contribution to health and security of Japanese citizens based on Safety Triangle

Relief benefits service for health damage	Review service	Safety measures
➢ Enhance publicity and dissemination of information to ensure the use of relief service ➢ Prompt response to claims for benefit	➢ Keep review time at the world's fastest level and further improve its higher quality ➢ Proper operation of SAKIGAKE Designation System and Conditional Early Approval System ➢ Conduct RS Strategy Consultations, etc. ➢ Address utilization of RWD in submissions	➢ Promote safety assessment based on drug epidemiological survey using medical information database ➢ Rapid identification and assessment of ADRs/malfunctions ➢ Promote ADR reporting from medical institutions and more use of ADR information from patients ➢ Promote utilization of safety information in clinical practice

2． Cross-organizational activities to support and further advance Safety Triangle

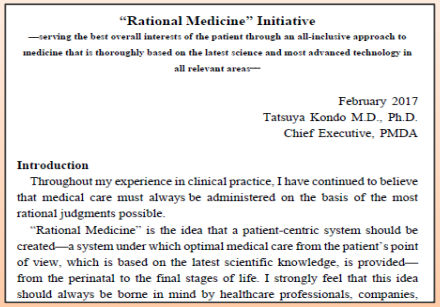
Improvement of service quality by promoting RS	Globalization	Operations
➢ Establish horizon scanning method ➢ Promote advanced evaluation method ➢ Improve quality of benefit-risk assessment using medical information database ➢ Develop organizational structure that promotes the use of MID-NET®	➢ Take global leadership ➢ Strengthen bilateral cooperation and Asia Training Center ➢ Announce PMDA's activities actively and globally	➢ Develop the governance and compliance system based on PMDA's role and social position ➢ Secure and develop qualified human resources and further enhance service quality

Dr. Fujiwara's Priorities

< 4Fs >

- ◆Patient **F**irst
- ◆Access **F**irst
- ◆Safety **F**irst
- ◆Asia **F**irst

by Fujiwara



"Rational Medicine" Initiative

—serving the best overall interests of the patient through an all-inclusive approach to medicine that is thoroughly based on the latest science and most advanced technology in all relevant areas—

February 2017
Tatsuya Kondo M.D., Ph.D.
Chief Executive, PMDA

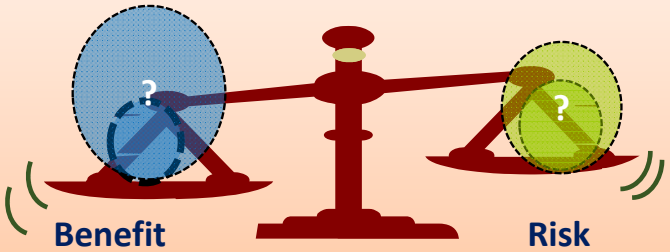
Introduction

Throughout my experience in clinical practice, I have continued to believe that medical care must always be administered on the basis of the most rational judgments possible.

"Rational Medicine" is the idea that a patient-centric system should be created—a system under which optimal medical care from the patient's point of view, which is based on the latest scientific knowledge, is provided—from the perinatal to the final stages of life. I strongly feel that this idea should always be borne in mind by healthcare professionals, companies,

"Rational Medicine" Initiative

by Kondo



Regulatory Science

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Dr. Fujiwara's Priorities

◆Patient First

Improve **patient satisfaction** by learning what is happening around the clinical settings

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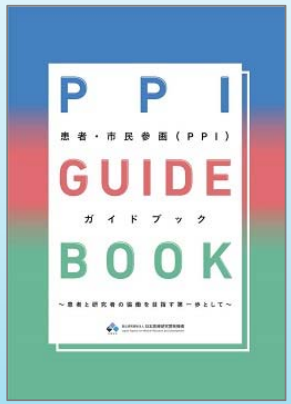
Patient Engagement

Initiatives at Japan Agency for Medical Research and Development

Committee chair for research on **patient and public involvement (PPI) in clinical trials**

(conducted during 2017.07-2019.03)

- Definition, mission and basic principles of PPI were established
- PPI Guidebook was developed and published in Apr, 2019
- Report will be published soon



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Patient Engagement
Initiatives within PMDA

日刊薬業 60th

2019年5月31日（金）

新生PMDAが本格始動、「患者参画WG」立ち上げ　藤原新理事長が指示　審査・安全対策に意見反映へ

2019/5/31 04:30

初の単独取材に応じる藤原新理事長

医薬品医療機器総合機構（PMDA）の藤原康弘新理事長は30日、日刊薬業の取材に応じ、就任時に全役職員に指示した“4つのF（ファースト）”の実現に向けた具体的な取り組みを始めたことを明らかにした。その一つ、「ペイシェント・ファースト」では、医薬品の審査や安全対策に患者の意見が反映されるようにするための方策などについて検討する「患者参画ワーキンググループ（WG）」を新設した。2年後をめどに成果をまとめる方針だ。ほかの

In May 2019, PMDA established **Patient Centricity Working Group** to:

- discuss how patients can be involved in PMDA's **review** and **safety** services
- develop and publish **guidance and principles** on PPI at PMDA

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Dr. Fujiwara's Priorities

◆Access First

- Ensure **appropriate risk-benefit balance**
- **Accelerate the access** to innovative medical products of public demand

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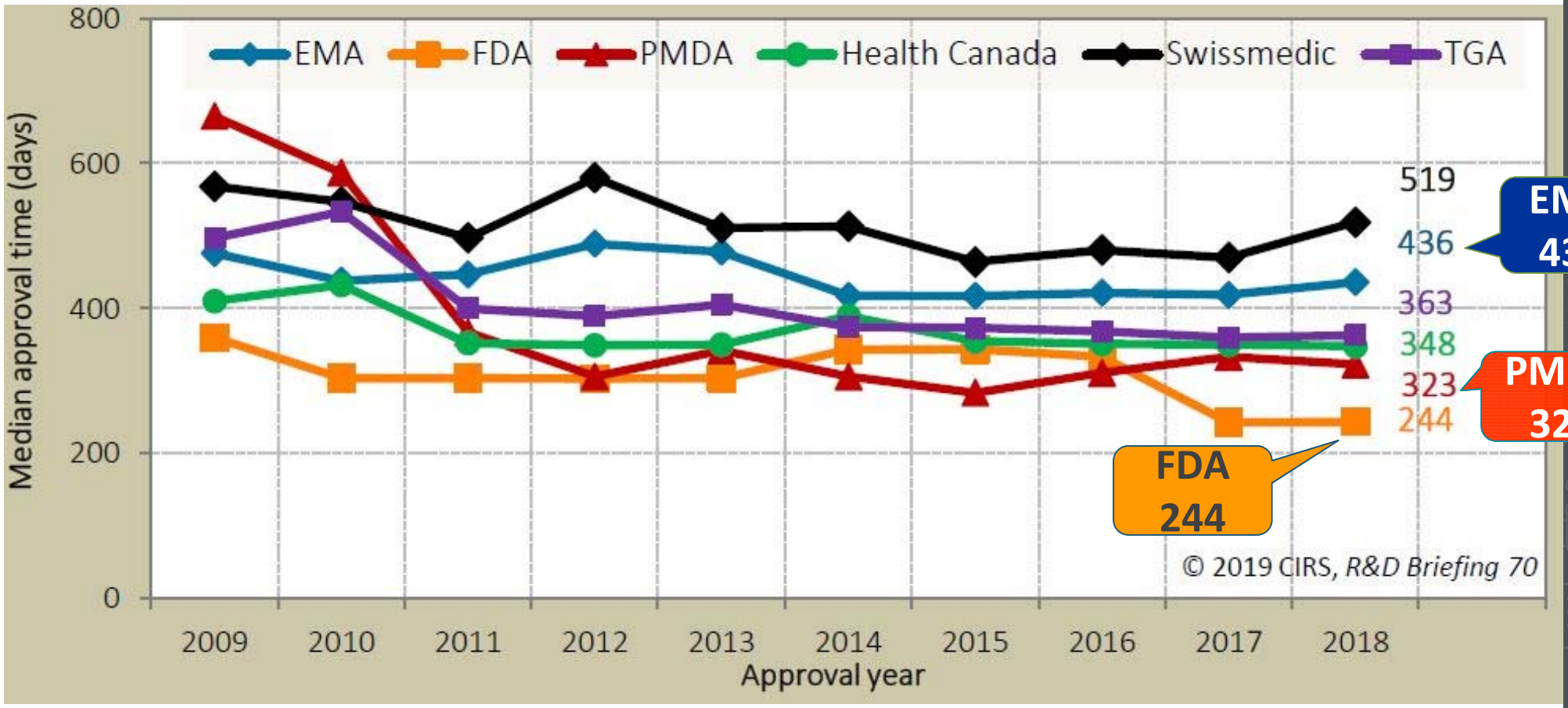
New active substance (NAS) median approval time among six regulatory authorities in 2009-2018 (Pharmaceuticals)



Approval time is calculated from the date of submission to the date of approval by the agency.
This time includes agency and company time. EMA approval time includes the EU Commission time.

Centre for Innovation in Regulatory Science (CIRS) , 2019, R&D Briefing 70

Challenges - Low IBD in Japan -

The NEW ENGLAND JOURNAL of MEDICINE

CORRESPONDENCE

Regulatory Review of New Therapeutic Agents — FDA versus EMA, 2011–2015

TO THE EDITOR: The Food and Drug Administration (FDA) faces continual pressure to accelerate the regulatory review and approval of new medicines. Although the 21st Century Cures Act, which was signed into law in December 2016, includes several reforms that are intended to further streamline FDA evaluations,[1] the speed of the regulatory review process is directed by the Prescription Drug User Fee Act (PDUFA).[2] With Congress poised to consider the reauthorization of the PDUFA before it expires in October 2017, the speed of the FDA regulatory review process will come under renewed scrutiny. To inform these discussions, we compared review times for new therapeutic agents that were approved by the FDA or the European Medicines Agency (EMA), the primary drug regulator in Europe, between 2011 and 2015.

Using methods similar to our previously published comparison of agency review times,[3] we identified all the new therapeutic agents that had been approved by the FDA or the EMA between 2011 and 2015, classifying them according to therapeutic area and orphan status. Next, we abstracted key regulatory dates and com-
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THIS WEEK'S LETTERS

RESPONSE

The authors reply: Fujiwara and Ono describe regulatory review times for drugs ap
Japan's regulator, the PMDA. Although the PMDA appears to be conducting regula
promptly, research suggests that from 2008 through 2014, only 5% of new therape
were submitted to the PMDA before submission to the U.S. Food and Drug Admini
European Medicines Agency.[1] This low submission rate may have allowed the PMD
making its evaluation, to leverage regulatory experience with regard to these new t
agents that were first considered in the United States and Europe.

The PMDA places particular emphasis on data collected from the Japanese populat
delayed submission to this agency probably reflects the need to ensure that a suffic
of Japanese patients are included in the clinical evaluation programs, which can ent
clinical trials.[2] Nonetheless, the PMDA has made remarkable progress in accelerating
of its regulatory review process,[1] and these new data suggest that the review times of the
are similar to those of other leading drug regulators.

Nicholas S. Downing, M.D.
Brigham and Women's Hospital, Boston, MA

Audrey D. Zhang, A.B.
New York University School of Medicine, New York, NY

Joseph S. Ross, M.D., M.H.S.
Yale School of Medicine, New Haven, CT
joseph.ross@yale.edu

Since publication of their letter, the authors report no further potential conflict of interest.

Author's response: "**only 5% of new therapeutic agents were submitted to the PMDA** before submission to the U.S. FDA or the EMA."

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Regulatory Action towards Access First

- SAKIGAKE Designation System
- Conditional Early Approval System
- Real World Data Utilization
- International Collaboration

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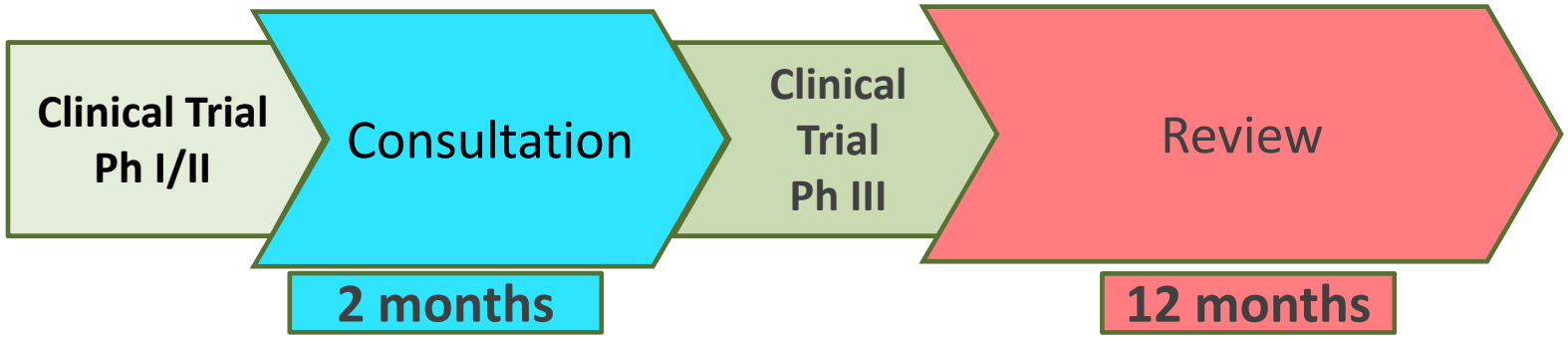
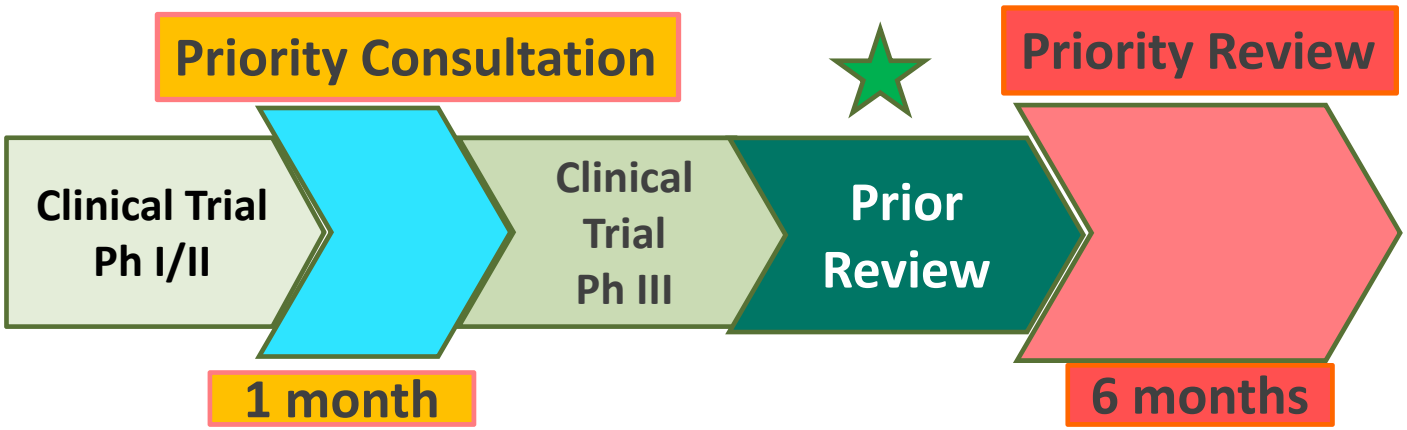
SAKIGAKE Designation System

【Ordinal Review】



【SAKIGAKE 】



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PMDA's Efforts Toward Utilization of Real-World Data (RWD)

1. New Consultation Category for Registry Utilization (piloted in FY2019)

- Multiple consultation categories for registry holders and product developers
  - For registry holders
    - General considerations to ensuring reliability of registry data for regulatory approval
  - For product developers
    - Advice on the development plan using registry and the reliability of the registry data for individual product

2. Preparation of Guideline for Product Development utilizing RWD

- Notification issued
  - Amended GPSP Ordinance
  - Basic Principle for Utilization of Medical Information Database in Post-Marketing Pharmacovigilance (2017.6.9)
  - Points to Consider for Ensuring the Data Reliability on Post-Marketing Database Study for Drugs (2018.2.21)
  - Points to Consider for Ensuring the Data reliability on Post-Marketing Database Study for Medical Devices (2018.12.19)
- **Basic principle for utilization of registry data for regulatory submission and points to consider for ensuring the data reliability are being developed**, considering experience from consultations and global circumstance.
  - **Drafts will be developed in FY2019**, and their finalization/publication is planned in FY2020 after discussion with experts.

Finalization/ publication is planned **in FY2020**

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International Collaboration for Early Patient Access

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MHLW/PMDA's participation in ICMRA

- Member of the ICMRA Executive Committee
- Former project lead of the ICMRA Innovation Project WS1: Horizon Scanning, Methodology and Best Practice
- Maintenance and update of the ICMRA public website
- Active participation in nearly all projects and initiatives

Innovation Project Meeting in Tokyo

ICMRA Public Website (www.icmra.info)

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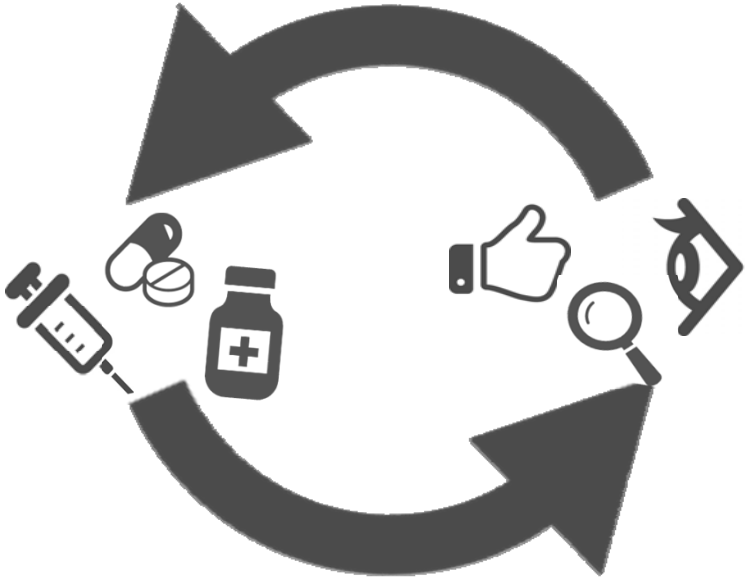
Dr. Fujiwara's Priorities

◆Safety First

Implement **efficient post-marketing data collection** and **product distribution control**, especially for accelerated approval scheme



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Conditional and Time-limited Approval of Regenerative Medical Product

Conventional Approval Process

Regulatory System that Facilitate Early Patient Access

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PMDA-Qualified Real World Data

Medical Information Database Network (MID-NET)

- Promote safety measures by pharmaco-epidemiological method using medical information database.
- MHLW/PMDA have established a medical information database for collecting large-scale medical data at sentinel site hospitals and have constructed analytical systems at PMDA since FY 2011.

MID-NET

Researcher, MAHs

Collaboration

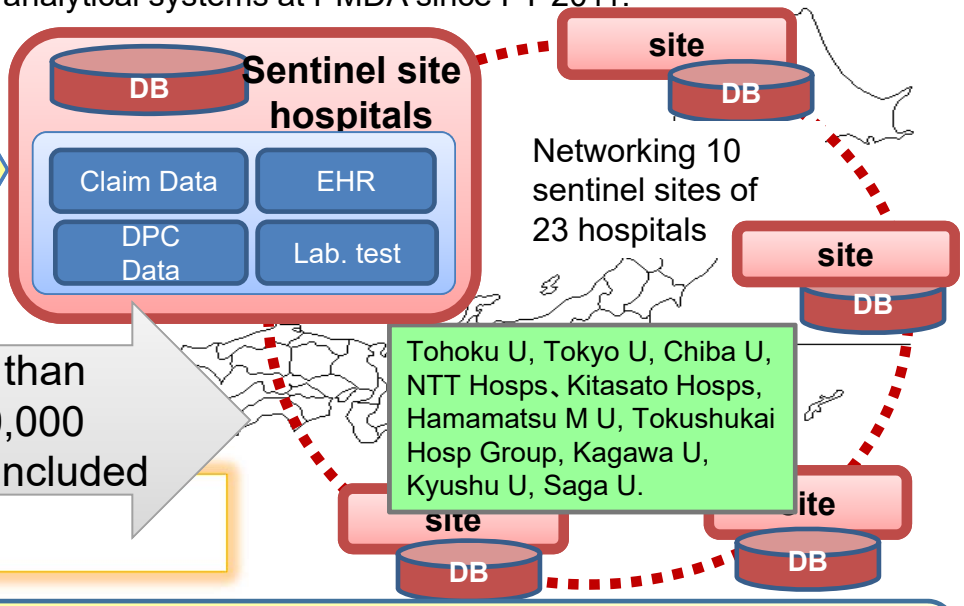
PMDA
safety information collection and analysis

Data analysis

Prompt safety action

More than 4,000,000 patients included

Expected Outcome：
Prompt and precise safety actions



【History and way forward】

- ●April 2010 :「Revision of pharmaceutical administration etc. to prevent recurrence of pharmaceutical disasters (final recommendation)」
- ● April 2011 - : Start construction of MID-NET system
- ● April 2013 - : Start data quality validation to assure precision and comprehensiveness of the collected data
- ● April 2015 - : Start trial operations by PMDA and sentinel sites
- ● April 2015 - : Setting utilization rules for full-scale operation and framework of operation cost / user fees.
- ● April 2018- : Full scale operation, enable MAHs and researchers to use MID-NET

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Summary of studies published

ORIGINAL REPORT

WILEY

The utilization and challenges of Japan's MID-NET® medical information database network in postmarketing drug safety assessments: A summary of pilot pharmacoepidemiological studies

Kaori Yamada[1] | Maori Itoh[1] | Yoshiaki Fujimura[2] | Michio Kimura[3] | Koichiro Murata[4] | Naoki Nakashima[5] | Masaharu Nakayama[6] | Kazuhiko Ohe[7] | Takao Orii[8] | Eizaburo Sueoka[9] | Takahiro Suzuki[10] | Hideto Yokoi[11] | Chieko Ishiguro[1] | Yoshiaki Uyama[1] | on behalf of MID-NET® project group

Abstract

Purpose: To examine the potential role of Medical Information Database Network (MID-NET®), a newly established Japanese medical information database network, in postmarketing drug safety assessments through the characterization of its advantages and limitations in five pilot studies.

Methods: The pilot studies were designed to address three major objectives in postmarketing drug safety assessments, ie, the examination of actual drug utilization, the impact of safety-related regulatory actions, and drug-associated risks. The five studies were conducted on the following topics: (a) utilization of codeine-containing products and its relationship with respiratory depression, (b) impact of a Dear Healthcare Professional letter on hypocalcemia incidence associated with denosumab (Ranmark®) use, (c) risk of acute myocardial infarction associated with antidiabetic drug use, (d) risk of glucose metabolism disorders associated with atypical antipsychotic drug use, and (e) prospective monitoring of abnormal laboratory test results

Pharmacoepidemiol Drug Saf. 2019;28:601–608

Dear Healthcare Professionals Letter of Rapid Safety Communication

- Brand Name:
  Verzenio 50mg, 100mg, 150mg (abemaciclib)
- Letter issued on:
  May 17, 2019
- Safety Information:
  14 serious cases of interstitial lung disease reported in patients treated with Verzenio Tablets in Japan

Health care professionals are requested to pay careful attention to use this drug

IMPORTANT

May 2019 No.19-01

Dear Healthcare Professionals Letter of Rapid Safety Communication
BLUE LETTER

Serious Interstitial lung disease by Verzenio Tablets 50 mg, 100 mg, 150 mg.

Since their launch in Japan on November 30, 2018, 14 serious cases of interstitial lung disease have been reported in patients treated with Verzenio Tablets 50 mg, 100 mg, or 150 mg (hereinafter referred to as "this drug") in Japan as of May 14, 2019 under the early post-marketing phase vigilance of the drug. Three of the 14 cases were reported as resulting in mortality (the estimated number of patients using this drug is approximately 2 000*). To address the situation, it has been decided that a Warning section should be newly added for a cautionary statement to the Precautions in the package insert for Health care professionals (hereinafter referred to as "HCP ") of this drug for alerting purpose.

*Estimated for a period from the start of marketing to May 14, 2019.

HCPs are requested to pay careful attention to the following points when using this drug.

- When administering this drug, patients should be carefully monitored for initial symptoms of interstitial lung disease (such as dyspnoea, cough, and pyrexia) and by performing a chest X-ray, etc.
- If any abnormalities are observed, administration of this drug should be discontinued and appropriate measures should be taken while performing a chest CT scan or serum marker test, etc. as necessary.
- Patients or their families should be instructed to immediately contact their physicians or pharmacists when they experience any initial symptoms of interstitial lung disease (such as dyspnoea, cough, and pyrexia).

Please note that the Warning, Important Precautions, and Clinically Significant Adverse Reactions sections have been revised.

Refer to Page 3 for contact information.

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Dr. Fujiwara's Priorities

◆Asia First

- Promote **regulatory harmonization** and improve **public health** among Asian countries/regions

- Further build **trust** in Japanese regulatory system

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Asia First

Similarities in:

- geography
- genetics
- cultures

Streamlined product development

Access to all Asian population around the world

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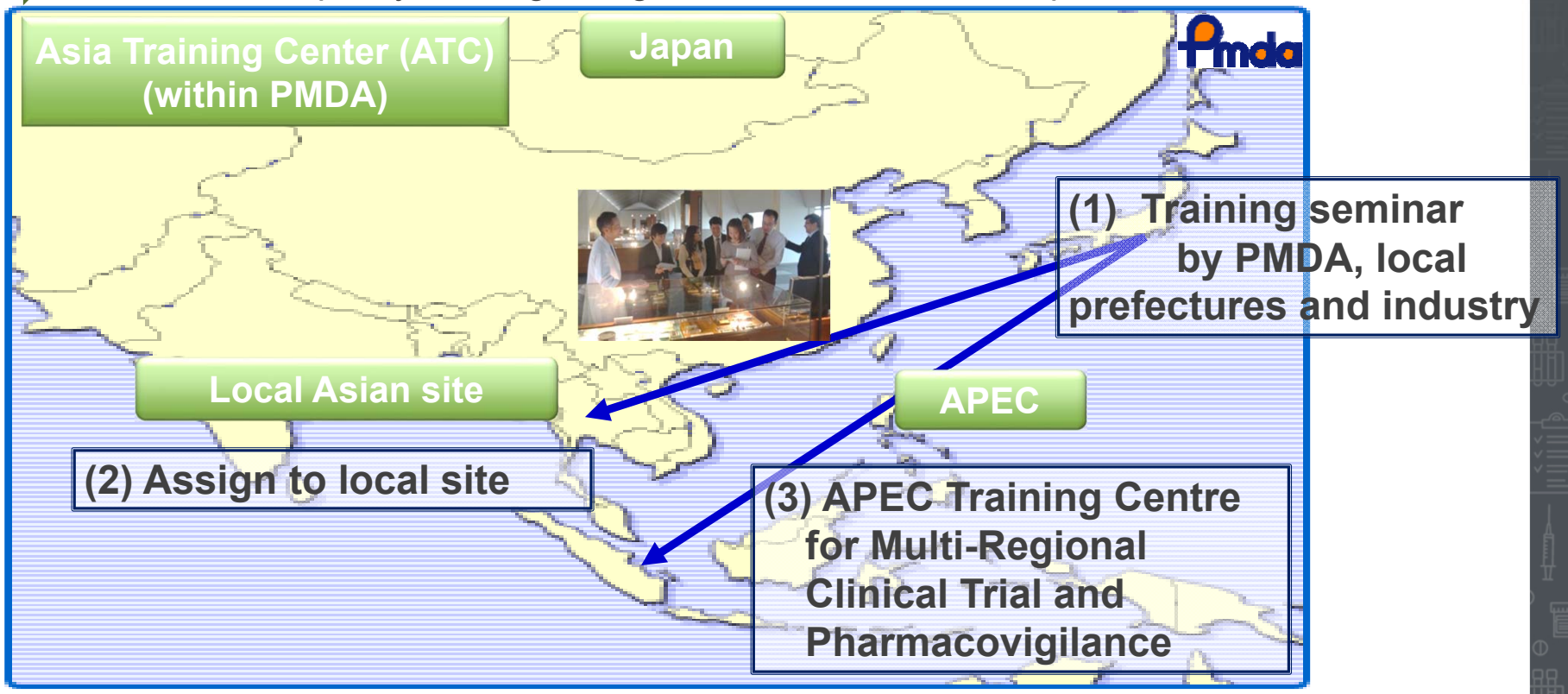
Asia Training Center for Pharmaceuticals and Medical Devices Regulatory Affairs (PMDA-ATC, est. April 2016)

- Plan, design and coordinate training for regulators in Asia and other parts of the world
- Provide **training opportunities** including **on-site training**

Attendees (FY 2018)
10 training seminars
267 attendees
from **31** countries/regions

➡ Contribute to capacity building of regulators in Asia and other parts of the world



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The Future of PMDA

Patient First

Safety First

Pmda

Asia First

Access First

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Thank You

The Future of PMDA

Yasuhiro Fujiwara, M.D., Ph.D.
Chief Executive, PMDA

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