Messages for the 10th Memorial Round Table

Future Drug Development and Regulatory Science

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PMDA’s Role: Three Major Services

~ Safety Triangle ~

Review
Reduction of risk

Safety
Continuous risk mitigation efforts

Japanese citizens

Relief
Relief measures for adverse health effects

Three-pillar System to assure public safety
Proud system unique to Japan
### Strategies and Measures for PMDA Innovation

<table>
<thead>
<tr>
<th>Issues with PMDA (past 5 years)</th>
<th>Basic policies to address the issues</th>
<th>Efforts made so far</th>
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<tr>
<td>◆ Shorten review time</td>
<td>◆ Philosophy (Mission Statement)</td>
<td>● Increase staffs</td>
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<tr>
<td>・ Reduce drug lag</td>
<td>◆ Regulatory science</td>
<td>● Enhance training program</td>
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<tr>
<td>・ Reduce device lag</td>
<td>◆ Global partnership (Win-Win Relationship)</td>
<td>● Academic cooperation</td>
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<td>◆ Strengthen and enhance safety measures</td>
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<td>○ Science Board</td>
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<td>○ Joint Graduate School Program</td>
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<td>○ Human resource exchange program</td>
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#### Efforts made so far
- Increase staffs
- Enhance training program
- Academic cooperation
  - Science Board
  - Joint Graduate School Program
  - Human resource exchange program
- Industry-Government-Academia collaboration
- Pharmaceutical affairs consultation
- Cross-sectional project within PMDA
- IT-based safety measures
  - MIHARI Project
  - Project for developing medical information database infrastructure
- Risk Manager (RM)
- Risk Management Plan (RMP)
- GLP, GCP, GMP, QMS inspection programs
- Adverse health effect relief system
- International strategic plan
- International liaison officers to US and EU
- Global partnership with US, EU and Asian countries (ICH, IMDRF, PIC/S, etc.)

**Pharmaceutical affairs are the ultimate medical ethics, and regulatory science is the underlying science.**
PMDA continues to improve the public health and safety of our nation by reviewing applications for marketing approval of pharmaceuticals and medical devices, conducting safety measures, and providing relief to people who have suffered from adverse drug reactions.

We conduct our mission in accordance with the following principles:

• We pursue the development of medical science while performing our duty with greater transparency based on our mission to protect public health and the lives of our citizens.

• We will be the bridge between the patients and their wishes for faster access to safer and more effective drugs and medical devices.

• We make science-based judgments on quality, safety, and efficacy of medical products by training personnel to have the latest technical knowledge and wisdom in their field of expertise.

• We play an active role within the international community by promoting international harmonization.

• We conduct services in a way that is trusted by the public based on our experiences from the past.
Japan’s performance on NDA review

Japan authority have achieved the target on review, 12 months for standard review and 9 months for priority review as median, in the mid-term plan of PMDA for 2009-2013. Now it has the world’s highest performance.

* An average derived from Thompson Reuters IDRAC database
** CIRS 2010-2011 benchmark
GAP between expectation and Reality

Concerns and Needs for medical services

Traditional Science

Current Issues
- SAE after approval, Lower success rate, Insufficient risk communication, Uncertainty for decision

Advancing Regulatory Science

New study design and analytical tool

Predictable model for efficacy/safety

New approach on risk communication and management

Objective evaluation tool for benefit/risk assessment

Ensure Social Balance

Medical Needs

Regulatory Science

Traditional Science
Roles of Regulatory Science in drug development
Figure 1 The regulatory science “bridge” as a means to introduce products of science to patients and to society. Regulatory science performs three functions: providing tools for data production, a basis for data assessment, and methods for balancing various factors. All three functions are indispensable to a proper introduction of a new product of science (here, "Drug A").

Details of 3 Factors in Regulatory Science

- Higher efficiency
  - Biomarker
  - M&S
  - Adaptive Design
  and more

- Higher quality
  - Objective and Quantitative assessment etc.
    - What is Benefit?
    - What is safety?

- Better balance
  - Better methods for benefit/risk assessment
  - Medical and social needs
  - Patients voice
  and more
Micro-Perspective in Regulatory Science

Assessing data of a study

• For example,
  – Efficacy evaluation based on “primary endpoint”
  – Safety evaluation based on dose-adverse event relationship

Microscopic observation
Macro-Perspective in Regulatory Science

Value to the Society in promoting the Health

Scientific, Non-bias, Objective,
Evaluation based on Regulatory Science

Truth

10th Annual Meeting DIA Japan 2013
November 6-8 | Tokyo
Engineering Drug Development

Multidisciplinary Expertise in Regulatory Science

Practical Drug Use

Regulatory Science Tree

Sociology

Education

Economics

Technological Science

Medical Science

Business Administration

Agricultural Science

Veterinary Medicine

Biostatistics

Pharmaceutical Science

Jurisprudence

and More

Seeds for a drug

Ethics
PMDA initiatives to Advance Regulatory Science
Basic Research

Seeds of medical products discovered in Japan

Discovery in Basic research e.g.; iPS

Non-Clinical

Clinical

NDA

Approval

Post Market

PMDA

Pharmaceutical Affair Consultation

Scientific Consultation

Review

Safety Measure

Offices of Review; Drugs, Biologics, Medical Devices, Offices of Safety

Office of Review Innovation

Science Board

Board Member

Academia

Practical Use

Innovative Medical Products

e.g.; HAL

iPS-derived products

10th Annual Meeting DIA Japan 2013
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Collaborative Graduate School Program

- PMDA Staff
  - Visiting Professor (Lecture in regulatory science)
  - Graduate student (Ph.D. program); Research in University

  The agreement with 18 Universities (as of October 2013)

- University student
  - Graduate student (Ph.D. program); Research in PMDA
Regulatory Science Research & Human Resource Exchange Program
(for developing innovative drug, device, cell & tissue products for practical use)

Pharmaceuticals and Medical Devices Agency

Human Resource Exchange & Development

Reviewer

Researcher

Acadia (University, Institute, Hospital)

Training in regulatory science

Effective research & development for regulatory approval

Outcome of research

Learning a state-of-the-art technology

Improving a quality of review and other services in PMDA

- Proactive establishment of the guideline and standards
- Promoting development using innovative techniques
Advanced workflow of review/consultation using innovative assessment techniques

- Analysis by PMDA
  - Giving additional scientific value to submitted data

- Cooperation with Academia

- Regulatory Science
  - Practical use of Innovative Medical Products
  - A rational & effective evaluation process for regulatory decision

- NDA etc.
  - e-Submission of study data
  - Database
  - Accumulation of data

- Sophisticated NDA review
  - Innovative assessment techniques
    - Comprehensive analysis of stratified data

- Cross-Products Analysis
  - Innovative evaluation methods
  - Active utilization of Modeling & Simulation
    - Disease model
    - Objective B/R assessment
    - Identifying AE-related factors etc.

- Sophisticated Consultation
  - More evidence-based consultation

- Effective and High Quality Review
  - More predictable efficacy/safety after approval
  - Reduction of applicant’s work load
  - More scientific regulatory decision

- Effective and Successful Development
  - Epoch-making proposal leading the world
  - Proactive publication of guideline
More comprehensive and stronger “Regulatory Science Bridge” will help us develop a drug in the future

Toward Global PMDA

- Offer an innovative medicine based on Japanese technology to the World
- Advancing Regulatory Science through International Collaborations

Safety

Japanese citizens

Review

Relief

Contribute to Global Health
Thank you for your attention

ご清聴ありがとうございました

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감사합니다