PMDA’s Future Activities

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"Rational Medicine" Initiative

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"Rational Medicine" Initiative

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, government authorities, and all other parties concerned.

The Pharmaceuticals and Medical Devices Agency (PMDA) is, of course, proud to be a key player among these parties. As given in the Mission Statement I made public upon assuming the post of Chief Executive, PMDA has striven to conduct its review, safety and relief service operations based on its mission "to protect public health and the lives of our citizens", to "develop its human resources so that they possess the latest expertise and wisdom in their areas of expertise", and to combine their strengths so as to "make thoroughly appropriate, science-based judgments on the efficacy and safety of medical products".

In seeking to make a holistic approach to medicine—an approach that takes the whole spectrum of considerations to account in order to serve the best overall interests of the patient, not just the specialist’s view in a defined area of expertise—the norm, PMDA is pursuing two more specific aims. The
What is the “Rational Medicine”?  

A patient-centric system
• from the perinatal to the final stages of life
• based on the latest scientific knowledge
• provide a holistic approach to medicine

All concerned parties including healthcare professionals, medical companies, and government authorities work hard to realize the Idea.
Develop new evidence of evaluation methods to evaluate quality, efficacy, and safety of medical products, based on discussions at the PMDA’s Science Board

- Make our citizens access earlier to medical products using innovative new technologies which has only just become available
- Provide optimal medical treatment as benefits of Rational Medicine
Initiatives of PMDA to Rational Medicine

1. Promotion of innovation by improving quality and rationality of review process
2. Further promotion of regulatory science
3. Increased sophistication of safety measures through the use of real-world data
4. Enhanced international partnerships

All PMDA work its upmost for Rational Medicine
1. Innovation through product approval reviews of enhanced rigor and rationality

- Utilize electronic application data (of new drugs) in individual product reviews
- Advance discussions on enhancing the speed of medical device review
- Further enhance its Pharmaceutical Affairs Consultations on R&D Strategy and other consultation services
- Further shorten review times through SAKIGAKE Designation System
- Support for the practical application of innovation gains
CDISC Data Submission [NDA]

- **NDA Review**: More effective & High level review
  - B/R evaluation with raw data analysis
- **Scientific Consultation**: More efficient & Successful development
  - Scientific advices based on the information obtained from analyses including M&S
- **Cross-Products Analysis**: More evidences & Advancing Regulatory Science
  - Establish disease models
  - Identifying common risk factors among different drugs

Modeling & Simulation: Concentration-Response
Model PBPK: Physiologically-based Pharmacokinetic Model, etc.
Enhancement of Pharmaceutical Affairs Consultation on R&D Strategy

- Facilitate development of medical products by academia by developing more reliable ROADMAP.
- Contribute to promotion of clinical trials led by academia.

Advice on ROADMAP

Advice on protocol of each study

Quality study

Non-clinical study

Clinical study

Exploratory trial

Confirmatory trial

Basic Research

Promising seeds

Practical Use

Innovative drugs, medical devices, and regenerative medical products

Bridge between seeds and products

* In collaboration with the Japan Agency for Medical Research and Development (AMED), PMDA will proactively support establishment of an exit strategy via Pharmaceutical Affairs Consultation on R&D Strategy.
**SAKIGAKE - General Timeframe**

**Ordinary Review**

- Non-clinical
- Phase I/II
- Phase III

**SAKIGAKE**

- Designation
- Prior Review
- Review

**Consultation**

- 2M
- 6M
- 12M

**Designated in 1st round pilot (FY2015)**

- 6 Pharmaceuticals
- 2 Medical Devices
- 3 Regenerative Products
SAKIGAKE (1st round) and Pharmaceutical Affairs Consultation on R&D Strategy (Concept)

Preliminary Review & Evaluation
1. Innovative medical products
2. For serious diseases
3. Development & NDA in Japan being world’s first or simultaneous with other countries
4. Prominent effectiveness expected on non-clinical and early phase clinical studies

SAKIGAKE process with priorities
SAKIGAKE Designation System Pilot (2nd round)

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<td>22</td>
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- **Step 1: Announcement & application period**
  - Announcement made on 10/3/2016, and receive applications from 10/3 – 11/22/2016
  - Started interview on applied products.

- **Step 2: Interview on applied products**
  - Preliminary review, PMDA’s evaluation and final judgment for designation by MHLW

- **Step 3: Evaluation and designation**
  - Finalize designated products by designation standards in consideration with preliminary review when necessary and PMDA’s evaluation.

**Timeline:**
- Announcement made on 10/3/2016, and receive applications from 10/3 – 11/22/2016
- Started interview on applied products.

**Interview on applied products**
- Announcement of Designated products

**SAKIGAKE Designation System Pilot (2nd round)**
### 2nd Round of *SAKIGAKE* Designated Products
- **Regenerative Medical Products** -

<table>
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<tr>
<th>Name of product</th>
<th>Summary of product</th>
<th>Name of applicant</th>
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| **CLS2702C/D**  
 (Oral mucosa-derived esophageal cell sheet)                              | Shorter re-epithelialization period after extensive endoscopic submucosa dissection (ESD) in esophageal cancer. | **CellSeed**  
 *(Seeds: Tokyo Women’s Medical University Hospital)* |
| **Dopamine neural precursor cell derived from non-autologous iPS cell**  
 (Therapeutic stem cell for Parkinson’s disease) | Novel therapy by inducing dopamine discharge to mitigate neural symptoms of patients with Parkinson’s disease. | **Sumitomo Dainippon Pharma Co., Ltd.**  
 *(Seeds: Center for iPS Cell Research and Application, Kyoto University)* |
| **Pluripotent progenitor cell derived from human (allogeneic) adult bone marrow**  
 (Stem cell suspension derived from adult marrow)                              | Novel therapy for improving functional impairment caused by acute brain infarction.                  | **Healios K.K.** in Japan  
 **Athersys** (US company) outside of Japan |
# 2nd Round of SAKIGAKE Designated Products
- Medical Devices and *In-Vitro* Diagnostic-

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<th>Name of product</th>
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<th>Name of applicant</th>
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<tr>
<td>Artificial tracheal (made of polypropylene mesh and</td>
<td>Aiding reconstruction of tracheal while maintaining intratracheal structure after</td>
<td>Daiichi Medical&lt;br&gt;(Seeds: Kyoto University, etc.)</td>
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<td>collagen sponge)</td>
<td>partial removal.</td>
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<td>Boron neutron capture therapy (BNCT) system (Neutron</td>
<td>Selective destruction of tumor cells marked by boron agents, without damaging</td>
<td>Stella Pharma Corporation&lt;br&gt;Sumitomo Heavy Industries, Ltd.&lt;br&gt;(Seeds: Kyoto</td>
</tr>
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<td>irradiation system for BNCT)</td>
<td>normal cells.</td>
<td>University, etc.)</td>
</tr>
<tr>
<td>UT-Heart (Software program to aid prediction of</td>
<td>Higher accuracy of prediction of effectiveness of cardiac resynchronization therapy</td>
<td>Fujifilm Corporation&lt;br&gt;UT-Heart Inc. (A venture company by The University of Tokyo)</td>
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<tr>
<td>effectiveness of cardiac resynchronization therapy)</td>
<td>for patients with serious heart failure.</td>
<td></td>
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<tr>
<td>Cancer-related gene panel examination system</td>
<td>Collective examination of cancer-related genes to aid decisions on cancer treatment</td>
<td>Sysmex Corporation&lt;br&gt;(Seeds: National Cancer Center)</td>
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## 2nd Round of SAKIGAKE Designated Products

### Pharmaceuticals

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<tr>
<td>Olipudase Alfa (Genetical Recombination)</td>
<td>Acid sphingomyelinase deficiency</td>
<td>Sanofi K.K.</td>
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<tr>
<td>aducanumab</td>
<td>treatment and prevention of Alzheimer's Disease</td>
<td>Biogen Japan Ltd.</td>
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<tr>
<td>DS-5141b</td>
<td>Duchenne muscular dystrophy (who has a mutation of the dystrophin gene that is amenable to exon 45 skipping)</td>
<td>DAIICHI SANKYO CO., LTD.</td>
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| SPM-011※                         | • Recurrent malignant glioma  
• Unresectable local recurred head and neck cancer and advanced non squamous cell carcinoma | STELLA PHARMA CORPORATION          |
| Nivolumab (Genetical Recombination) | Biliary Tract Cancer                                                                | ONO PHARMACEUTICAL CO., LTD.      |

※Boron preparation for use with the “Boron Neutron Capture Therapy (BNCT) System” designated as a SAKIGAKE product on February 28, 2017.
2. Further promotion of regulatory science

- Establishment of a Regulatory Science Center in 2018
  
  The advocate of Regulatory Science
  Dr. Mitsuru Uchiyama
  (Deputy Director General, National Institute of Health Sciences in Japan, at the time)

- Formulation of guidelines to encourage the optimal use of novel medical products

- Discussions at PMDA’s Science Board to contribute to the introduction of innovative medical technologies
Science Board (Outcome Documents)

Major Outcome Reports

1\textsuperscript{st} term (FY2012 - 2013)

- Current perspective on evaluation of tumorigenicity of cellular and tissue-based products derived from induced pluripotent stem cells (iPSCs) and iPSCs as their starting materials (2013)

2\textsuperscript{nd} term (FY2014 - 2015)

- Report on the use of non-clinical studies in the regulatory evaluation of oncology drugs (2016)
1. Clinical evaluation of rare cancer
   - Discuss current situation of clinical evaluation and possible evaluation methods of disease areas in which efficacy of drug by comparative studies is difficult, such as in rare cancers, due to the number of patients is specifically limited among rare diseases (no more than 50,000 patients).

2. Facilitating R&D of Academia-originated Pharmaceuticals
   - Sort out problems of bottleneck of drug discovery in academia, and discuss their solutions.

3. Artificial Intelligence and its application in medical field
   - Discuss “totally new elements of AI” by overviewing new technologies using AI and facilitate them into future medical device review and consultations.

Outcome documents will be published in March, 2018.
4. Enhanced International Partnerships

- Provide trainings on MRCT and regulatory oversight of medical products
- Actively engaged with international regulatory coordination activities
- Organize “International Summit of Heads of Medicines Agencies” and a related symposium in Japan
# Lead the World in Regulatory Innovation

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<th>Stage</th>
<th>Agendas for PMDA</th>
<th>Activity</th>
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<tr>
<td>Development</td>
<td>○ Support for promising seeds to forward the development</td>
<td>➔ Pharmaceutical Affairs Consultation on R&amp;D Strategy (from July 2011)</td>
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<td>Review</td>
<td>○ Approaches to cutting-edge technologies (including iPS Cells by collaboration with Academia)</td>
<td>➔ Science Board (from June 2012)</td>
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<td>○ Support early practical use of Regenerative Medical Products</td>
<td>➔ Conditional Time-limited Authorization (from November 2014)</td>
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<td>○ Encourage Japan-first development and approvals</td>
<td>➔ SAKIGAKE Designation System (from FY 2015)</td>
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<td>○ Improve efficiency of development and review process by utilizing electric data</td>
<td>➔ Advanced review system (from October 2016)</td>
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<td>Post-marketing</td>
<td>○ Utilize medical information database to develop more sophisticated safety measures</td>
<td>➔ MIHARI project (from FY 2009)</td>
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<td>MID-NET project (under development)</td>
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Reform to rational and efficient structure based on Regulatory Science - to deliver more effective and safer drugs, medical devices, and regenerative medical products to clinical settings.
Innovative Product/Regulation from Japan to World

- Facilitating Innovation
- Faster Access of Patient to Innovative Products in Global Scale

Seeds of New Medical Products in Japan
Thank You

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