Japan Update

IMDRF Open Stakeholder Forum
March 2018
MHLW
Ministry of Health, Labor and Welfare

- Final Authorization of applications
- Publishing Guidelines
- Advisory committee
- Supervising PMDA Activities

PMDA
Pharmaceuticals and Medical Devices Agency

- Scientific Review for Drugs & MD
- GCP, GMP Inspection
- Consultation on Clinical Trials etc.
# Medical Device Regulations in Japan

<table>
<thead>
<tr>
<th>Classification</th>
<th>Class I</th>
<th>Class II</th>
<th>Class III</th>
<th>Class IV</th>
</tr>
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<tbody>
<tr>
<td>Category</td>
<td>General MDs</td>
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<td>Example</td>
<td><img src="image1.png" alt="Image" /></td>
<td><img src="image2.png" alt="Image" /></td>
<td><img src="image3.png" alt="Image" /></td>
<td><img src="image4.png" alt="Image" /></td>
</tr>
</tbody>
</table>

Post market safety (vigilance/surveillance) PMDA and MHLW

- **Classification**
  - Class I
    - General MDs
  - Class II
    - Controlled MDs
  - Class III
    - Specially controlled MDs
  - Class IV

- **Category**
  - General MDs
  - Controlled MDs
  - Specially controlled MDs

- **Premarket regulation**
  - Self-declaration
  - Third party certification
  - MHLW approval (PMDA review)

- **Example**
  - ![Image](image1.png)
  - ![Image](image2.png)
  - ![Image](image3.png)
  - ![Image](image4.png)
JAPAN UPDATE

1. Regulatory Science Center
2. AI
3. Sakigake Designation
4. Summit/ICMRA
Establishment of PMDA Regulatory Science Center

**Regulatory Science**: Science to predict, evaluate and determine quality, efficacy and safety of medicinal products *based on scientific knowledge properly and expeditiously*

Promotions So far... *Science Board, Joint Graduate School, Comprehensive Partnership Agreement, Cross-sectional Standards Development PT, etc.*

**Regulatory Science Center will be established in April 2018**, will actively collect and utilize scientific knowledge of quality, efficacy and safety especially derived from the “Real World Data” (such as MID-NET®)

- will improve the quality of review and safety measures
- will actively disseminate scientific evidence
- will actively publish guidelines

PMDA will be able to provide consistent assistance throughout the regulatory process from consultation to review and approval
Medical devices incorporating AI technology

Products incorporating Artificial Intelligence (AI)

→ Medical Devices or not: based on their use or mode of distribution

→ If YES: regulated by Pharmaceuticals and Medical Devices Act

**Medical Device Regulations**

- R&D, Clinical trials
- Product review
- Manufacturing quality assurance
- Distribution, Post-marketing safety measures

**Safety/Efficacy Evaluation**

**Efforts to date** → PMDA proactively engages

- Improved its consultation/review framework
  - to better recognize technological innovations (e.g. Robotics, ICT) (Oct. 2015)

- Issued a guidance document
  - to summarize key points on medical device programs review (e.g. diagnostic support) (Mar. 2016)

- Opinion exchanges
  - with diagnostic imaging devices developers (held since Dec. 2016)
1. Evaluation methodology

- **Evaluation considering characteristics specific to AI utilization**
  (e.g., continuous changes in product performance)

[MHLW] Expert Consultative Meeting on:

**Diagnostic imaging products (as first focus).**
- **Evaluation standards**
  - Outcome: by the end of Mar. 2018
  - Opinion exchanges with industry in parallel.

[PMDA] **Science Board - AI Subcommittee**

“AI as a New Factor in Medical Device Reviews”
- how to best adapt PMDA’s review/consultation services
2. Evaluation framework

- Post-marketing evaluations/follow-up requires sophisticated understanding
  - Characteristics/potential of AI (e.g., dynamism of processing capabilities)
  - Continuous evaluations/information provision: to Health Care Professionals

<possible next steps>

→ Prepare **suitable organizational structures** to be engaged in pre-/post-marketing evaluations

→ **Development/issuance of science-based guidelines prior to product development** with Regulatory Scientific Principles
SAKIGAKE Designation System

【Ordinal Review】
- Consultation
  - Non-clinical research / Clinical Research
  - Clinical Trial Phase I/II
- Consultation on Clinical Trial
  - 2 months
- Clinical Trial Phase III
  - 12 months
- Review
  - Covered by Insurance
  - Commercialization in market

【Review under SAKIGAKE Designation System】
- Priority Consultation
  - ① Priority Consultation
- Prior Review
  - ② Prior Review
  - 6 months
- Review Partner
  - ③ Priority Review
  - ④ Review Partner
- Prior Review
  - Designation as SAKIGAKE
  - Consultation on Clinical Trial
  - Clinical Trial Phase I/II
  - Clinical Trial Phase III
  - Covered by Insurance
  - Commercialization in market

Practical application of innovative medical products

⑤ Strengthening post-marketing safety measures (re-evaluation period)
### Designation of Sakigake products

Titanium Bridge, the first designated medical device submitted in June 2017, was reviewed in the priority review scheme and approved after only 6 months!

<table>
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<tr>
<th>No.</th>
<th>Product name</th>
<th>Expected performance/effectiveness</th>
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<tr>
<td>MD1</td>
<td><strong>Titanium Bridge</strong> (Hinge-type plate with titanium)</td>
<td>Adduction-type spasmodic dysphonia</td>
</tr>
<tr>
<td>MD3</td>
<td><strong>Artificial tracheal</strong> (made of polypropylene mesh and collagen sponge)</td>
<td>Aiding reconstruction of tracheal while maintaining intratracheal structure after partial removal.</td>
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<tr>
<td>MD4</td>
<td><strong>Boron neutron capture therapy (BNCT) system</strong> (Neutron irradiation system for BNCT)</td>
<td>Selective destruction of tumor cells marked by boron agents, without damaging normal cells.</td>
</tr>
<tr>
<td>MD5</td>
<td><strong>UT-Heart</strong> (Software program to aid prediction of effectiveness of cardiac resynchronization therapy)</td>
<td>Higher accuracy of prediction of effectiveness of cardiac resynchronization therapy for patients with serious heart failure.</td>
</tr>
<tr>
<td>IVD1</td>
<td><strong>Cancer-related gene panel examination system</strong> (Diagnostic system for DNA sequencer)</td>
<td>Collective examination of cancer-related genes to aid decisions on cancer treatment strategies.</td>
</tr>
</tbody>
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**First Approval of Sakigake Designation (December, 2017)**

One piece each at the upper and the lower parts of the thyroid to prevent involuntary glottal closure when speaking.

**Glottal opening width**

**Bridge**

**Wing**

**Glottal opening width**

**Bridge**

**Wing**
Summit of the Heads of Medicines Regulatory Agencies: started in 2006; consists of the heads of 23 regulatory agencies; chaired by a host country; and discusses the future vision of regulation (Regenerative Medical Products, Novel Information Databases, AMR, SSFFC .etc).

ICMRA (International Coalition of Medicines Regulatory Authorities): started in 2012; consists of 22 regulatory agencies; chaired by MHRA (UK) at present; and discusses strategically important areas (Crisis Management, Pharmacovigilance, and Supply Chain Integrity .etc).
Outcome of Kyoto Summit

1. Innovation
   - Regulatory convergence on regenerative medicines
   - Use of Real Word Data (RWD)

2. International Cooperation
   - Fight against Antimicrobial Resistance (AMR)
   - Countermeasures against substandard/falsified medical products
Thank you!