Japan Update

IMDRF Open Stakeholder Forum
September 2017
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>
</thead>
<tbody>
<tr>
<td>Category</td>
<td>General MDs</td>
<td>Controlled MDs</td>
<td>Specially controlled MDs</td>
<td></td>
</tr>
<tr>
<td>Premarket regulation</td>
<td>Self-declaration</td>
<td>Third party certification</td>
<td>MHLW approval (PMDA review)</td>
<td></td>
</tr>
<tr>
<td>Example</td>
<td><img src="image1" alt="Example" /></td>
<td><img src="image2" alt="Example" /></td>
<td><img src="image3" alt="Example" /></td>
<td><img src="image4" alt="Example" /></td>
</tr>
</tbody>
</table>

**Post market safety (vigilance/surveillance)**

- PMDA and MHLW

---

*Example images for each classification level are provided.*

---

*Textual content and diagrams related to medical device regulations in Japan.*
Registered Certification Bodies *(Ninsho-Kikan)*

As of Sep. 2017

| TÜV SÜD Japan |
| TÜV Rheinland Japan |
| DQS Japan |
| BSI Group Japan |
| SGS Japan |
| Cosmos Corporation |
| Japan Quality Assurance Organization (JQA) |
| Nanotec Spindler Corporation |
| Japan Electrical Safety & Environment Technology Laboratories (JET) |
| Japan Association for the Advancement of Medical Equipment (JAAME) |
| Fuji Pharma |
| DEKRA Certification Japan |
| Bureau Veritas Japan |
| Intertek Japan |

*Further information (in Japanese)*

http://www.pmda.go.jp/operations/shonin/info/attestation/ninsyokikan.html

http://www.jaame.or.jp/jyusho/ninjyu.html
(Reference) List of Certification Standards for Third Party Certification

Essential Principles Checklist with applicable standards
JAPAN UPDATE

1. Introduction of Conditional Early Approval Scheme
2. Introduction of SUD Reprocessing
3. Sakigake Designation
4. International Standard Approach
Conditional Early Approval for Innovative Medical Devices

Accelerate approval of MDs in high clinical needs by balancing the pre- and post-market requirements, based on the lifecycle management of the MDs.

- Collection of clinical data
- Review
- Approval
- Market - Use
- Conditional Early Approval for Innovative MDs
- Implementation of **Post-market Risk Management Measures**
- Data collection to confirm use results, long-term performance
Single-use Medical Device (SUD) Reprocessing

- Japan has introduced SUD Reprocessing from July 2017

- Reprocessers need MAH
- Reprocessed SUD needs Approval as R-SUD
- Reprocessers take responsibility for R-SUD's safety issue
SAKIGAKE Designation System

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

**[Review under SAKIGAKE Designation System]**
- Priority Consultation
- Prior Review
- 6 months
- Priority Review
- Review Partner
- Consultation as SAKIGAKE
- Non-clinical research / Clinical research
- Clinical Trial Phase I/II
- Consultation on Clinical Trial
- Clinical Trial Phase III
- Review
- 1 month

**Practical application of innovative medical products**

**5. Strengthening post-marketing safety measures (re-evaluation period)**
An **innovative MD/IVD for patients in urgent need of innovative therapy** may be designated as a Sakigake Product if:

1) its premarket application will be filed in the first in the world **AND**
2) prominent effectiveness can be expected.

Once an MD/IVD is designated, its developer can enjoy such benefits as:

A) Prioritized Consultation by PMDA

B) Pre-application substantive review

C) Prioritized Review
   (12 months ‡ 6 months [MD])

D) Review Concierge assigned by PMDA
### Designation of Sakigake products in 2016

The first designated medical device submitted application in June 2017. It will be reviewed in priority review scheme and will be approved within 6 months!

<table>
<thead>
<tr>
<th>No.</th>
<th>Product name</th>
<th>Expected performance/effectiveness</th>
</tr>
</thead>
</table>
| MD1 | Titanium Bridge  
(Hinge-type plate with titanium) | Adduction-type spasmodic dysphonia |
| RP1 | STR01  
(Autologous bone marrow-derived stem cells) | Improvement of neurological symptoms and functional impairment due to spinal cord injury |
| RP2 | G47Δ  
(Recombinant herpes virus) | Glioma |
| RP3 | Autologous intracardiac stem cells | Improvement of heart function in infants with congenital heart disease |
### Designation of Sakigake products

As of 28 February 2017, **7 more products** (3 medical devices, 1 IVD and 3 regenerative medicines) have been designated as Sakigake products.

<table>
<thead>
<tr>
<th>No.</th>
<th>Product name</th>
<th>Expected performance/effectiveness</th>
</tr>
</thead>
<tbody>
<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>
</tr>
<tr>
<td>MD4</td>
<td><strong>Boron neutron capture therapy (BNCT) system</strong></td>
<td>Glioblastoma, head and neck cancer; Selective destruction of tumor cells marked by boron agents, without damaging normal cells.</td>
</tr>
<tr>
<td></td>
<td>(Neutron irradiation system for BNCT)</td>
<td></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>
<tr>
<td>No.</td>
<td>Product name</td>
<td>Expected performance/effectiveness</td>
</tr>
<tr>
<td>-----</td>
<td>------------------------------------------------------------------------------</td>
<td>--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
</tbody>
</table>
| RP4 | **CLS2702C/D**  
(Oral mucosa-derived esophageal cell sheet) | Shorter re-epithelialization period after extensive endoscopic submucosa dissection (ESD) in esophageal cancer.                                                                                                                                |
| RP5 | **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.                                                                                                                                         |
| RP6 | **Pluripotent progenitor cell derived from human (allogeneic) adult bone marrow**  
(Sem cell suspension derived from adult marrow) | Novel therapy for improving functional impairment caused by acute brain infarction.                                                                                                                                                                |
Facilitate Development of International Standard for Evaluation method for Innovative MDs

To Enable early introduction of innovative MDs all over the world
I. Facilitate development of evaluation method (Practical, non-clinical, properly predict effectiveness and safety)
II. Facilitate development of such evaluation method into International Standard

Research
- Support research (Grant)
- Research Evaluation methods
- Propose Standard

Establish Evaluation methods
- MHLW
- Committee
  - Regulatory, Academia, Industry
  - Select project
  - Evaluate project
  - Support proposal of Standard

Develop Standard
- International Conference
- ISO, IEC, etc.

Support to selection of projects
- 2017-

Support Proposal of Standard
- 2018-
Thank you!