Regulatory Updates on Medical Devices in Japan

- Amendment of the Pharmaceuticals and Medical Devices Act (PMD Act)
- Software as a Medical Device (SaMD)

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Legal Structure for Medical Device

- Act
  - Pharmaceuticals and Medical Devices Act (PMD Act), 1960

- Cabinet Order
  - Cabinet Order on PMD Act, 1961
  - GCP/GLP for medical device, 2005
  - Good Vigilance Practice (GVP)
  - Quality Management System (QMS) etc.

- Ministerial Notification
  - Essential Principles
  - Certification criteria for class II/III devices
  - Classification of medical devices etc.

- Information on application procedures
  - Guidelines for clinical evaluation etc.
Definition of Medical Device in PMD Act

Medical devices are machinery or apparatus, etc. intended for use in the diagnosis, treatment or prevention of disease in humans or animals or intended to affect the structure or functions of the human or animal body, which are specified by Cabinet Order

Article 2.4, PMD Act
Intended use and claim

Perform stress analysis in various objects

Not intended to diagnose human disease

Medical indications such as diagnosis of bone fracture risk can not be claimed

Diagnose the risk of bone fracture from the results of stress analysis

Intended to diagnose human disease

Analytical performance to enable diagnosis of bone fracture risk should be evaluated

Not MD

MD
# 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>
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<tr>
<td>Premarket regulation</td>
<td>Self-declaration</td>
<td>Third party certification</td>
<td>MHLW approval (PMDA review)</td>
<td></td>
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<tr>
<td>Example</td>
<td><img src="image1.png" alt="Surgical tools" /></td>
<td><img src="image2.png" alt="Medical device" /></td>
<td><img src="image3.png" alt="Orthopedic devices" /></td>
<td><img src="image4.png" alt="In vitro diagnostic" /></td>
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</table>

**Post market safety (vigilance/surveillance)**: PMDA and MHLW
Under article 14-3 of the PMD Act, a certain medical product may be approved under when

① an emergency situation requires an unapproved medical product to be used to prevent damage to the public health caused by the spread of diseases

② such emergency situation cannot be managed appropriately by any means other than the use of the unapproved product, and

③ such product is legally available in a country with a regulatory system for medical products that is equivalent to Japan
Aim

• to enact a mechanism of early approval
  conditional, time-limited marketing approval may be granted in emergencies if the efficacy of the pharmaceutical, medical device, or regenerative medicine is estimated and safety is confirmed

• to enact a mechanism of electronic prescriptions

Outline

1. Marketing Approval in Emergencies
   New mechanisms to enable early marketing approval in emergencies.

   (1) Eligibility of pharmaceutical, etc. to which the early approval is applicable
   A pharmaceutical, etc. that needs to be used urgently in order to prevent the spread of a disease or other health hazard that could seriously affect the lives and health of people is eligible for early approval if there is no alternative existing treatment.

   (2) Application standards
   Assuming that safety has been confirmed, approval may be granted if the efficacy of the pharmaceutical, etc. has been estimated.

   (3) Conditions and term of approval
   As approval is granted at the early stage where efficacy has been estimated, conditions are provided to ensure the proper use of the pharmaceutical, etc. and restrictions are set in place that limit the duration of the approval to a short term.

   (4) Special measures to expedite review process
   Special measures are introduced for GMP inspections, national verifications as well as regulations on containers and packaging of the pharmaceutical, etc., in order to expedite review process for approval.

2. Creation of a mechanism for electronic prescriptions

Effective Date

The effective date (1. Marketing Approval in Emergencies): 20 May 2022
Transition of regulations for SaMD in Japan

before November 2014

program which determines performance of medical device

install

Medical device (tangible object including software)

after November 2014

Medical device (software itself)

install

MD software classified as Class I is NOT subjected to regulations on PMD-Act
The kind of Software treated as a Medical Device in Japan

Not Medical Device
- Not used for prevention, diagnosis or treatment of diseases

Software as a Medical Device (Class II〜IV)

Class I Software: Excluded from Medical Devices

- Probability and Significance of Risk
- Degree of Contribution to clinical decision

Not Medical Device
- Not used for prevention, diagnosis or treatment of diseases
## Overview of SaMD regulations

<table>
<thead>
<tr>
<th>Non-medical device</th>
<th>Medical device</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Not for diagnostics or treatment etc. corresponded to class I</strong></td>
<td><strong>Class II</strong></td>
</tr>
<tr>
<td>Programs for personal healthcare (ex: programs which give advice on meal or exercise for health maintenance and promotion)</td>
<td></td>
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<tr>
<td>Educational program (ex: training programs for health care professionals)</td>
<td></td>
</tr>
<tr>
<td>Programs corresponded to class I (ex: eye test, programs for color perception test)</td>
<td></td>
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<table>
<thead>
<tr>
<th><strong>For treatment</strong></th>
<th><strong>Program for therapy planning support</strong></th>
<th>61 items</th>
</tr>
</thead>
<tbody>
<tr>
<td>Application for behavioral therapy</td>
<td>1 item</td>
<td></td>
</tr>
<tr>
<td>Programmer for active implantable device</td>
<td>2 items</td>
<td></td>
</tr>
</tbody>
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<table>
<thead>
<tr>
<th><strong>For diagnostics</strong></th>
<th><strong>Program for computer assisted Imaging diagnostics</strong></th>
<th>263 items</th>
</tr>
</thead>
<tbody>
<tr>
<td>Program for computer assisted diagnostics other than imaging</td>
<td>71 items</td>
<td></td>
</tr>
<tr>
<td>Program for diagnostics assist for home use</td>
<td>2 items</td>
<td></td>
</tr>
<tr>
<td>Program for gene mutation analysis</td>
<td>7 items</td>
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</table>

Programs corresponded to class I (as of March 31, 2022): 2 items, 1 item, 263 items, 71 items, 7 items, 2 items.
Transition of number of approved SaMD

Number of approval

- Red: New MD
- Green: Improved MD with clinical data
- Blue: Improved MD without clinical data
- Yellow: Generic MD

as of March 31, 2022

Total number of approval:
- 2015: 9
- 2016: 13
- 2017: 19
- 2018: 19
- 2019: 36
- 2020: 43
- 2021: 39
- Total: 178
Examples of approved SaMD

(Ex. 1)
Digital Therapeutic App for Hypertension (approved on Apr. 2022)
→ Behavioral Approaches to Lifestyle Modification

(Ex. 2)
ELECTROCARDIOGRAPH SOFTWARE FOR OVER-THE-COUNTER USE (approved on Sep. 2022)
→ can provide information for identifying cardiac arrhythmias and encourage medical examination

(Ex. 3)
AI-Equipped Colorectal Endoscopy Diagnosis Support Software (approved on Dec. 2020)
→ Support for detection and differentiation of lesions in colonoscopy
Utilization of Post-Approval Change Management Protocol (PACMP)  
~Challenge to accept “Plasticity” in regulation~

Approval review process which enables continuous improvement of performance of SaMD using AI was introduced in September, 2020.

- Changes of performance must be in one-direction (improvement) and be managed by MAH.
- MAH may develop a process which ensures such performance changes “Improvement Process”, and submit to the approval review process.

Post-market changes in line with the Improvement Process can be made by notification, which does not require approval process.

*Compliance is checked in the audit.
<table>
<thead>
<tr>
<th>1. Early recognition of research seeds and publication of the review guide</th>
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<tr>
<td>a. Assess seeds of technology in the early stage of research.</td>
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<tr>
<td>b. Organize and publish the review guide regarding characteristics of SaMD.</td>
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<th>2. Centralization of the consultation contact desk</th>
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<td>c. Centralize consultation service (April 1, 2021)</td>
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<tr>
<td>d. Marshal and publish consultation case examples</td>
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<tr>
<td><a href="https://www.mhlw.go.jp/stf/seisakunitsuite/bunya/0000179749_00004.html">https://www.mhlw.go.jp/stf/seisakunitsuite/bunya/0000179749_00004.html</a></td>
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<th>3. Review system applicable to unique characteristics of SaMD</th>
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<td>e. Carry out efficient review based on characteristics of SaMD</td>
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<tr>
<td>f. Utilize the Post-Approval Change Management Protocol (PACMP) scheme</td>
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<td>g. Consider establishing the innovative SaMD designation program</td>
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<th>4. Enhancement of structure for early realization</th>
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<td>h. Establish new office specialized in SaMD in MHLW and PMDA (April 1, 2021)</td>
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<tr>
<td>i. Establish Expert Examination Committee for SaMD in the Pharmaceutical Affairs and Food Sanitation Council (April 1, 2021)</td>
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<td>j. Establish collaborative forum among regulator, academia and industry (February 4, 2022)</td>
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<tr>
<td>k. Enrich published database of approval cases</td>
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<tr>
<td><a href="https://www.pmda.go.jp/PmdaSearch/kikiSearch/">https://www.pmda.go.jp/PmdaSearch/kikiSearch/</a></td>
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Thank you for your attention

MHLW Website
https://www.mhlw.go.jp/english/

PMDA Website