The development of policy measures on medical devices using AI technology in Japan

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1. Key Definitions

2. Approval Review Principles

3. Guidance for evaluation on AI medical imaging systems

4. Legal Amendment for medical devices using AI technology
What kind of Software is Medical Device?

Class I Software:
Excluded from Medical Device

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

Software as Medical Device
(Class II~IV)

Degree of Contribution to clinical decision

Probability and Significance of Risk

Not used for prevention, diagnosis or treatment of diseases

low

high

Software as Medical Device

low

high

Class I Software: Excluded from Medical Device
Basic Act on the Advancement of Public and Private Sector Data Utilization (2016)

Article 2. Definitions
(2) The term "artificial intelligence-related technology" as used in this Act means technology for the realization of intelligent functions, such as learning, inference, and judgment, by artificial means, and utilization of the relevant functions realized by artificial means.
Reasons of Approval Rejection are common to all types of medical device.

(a) The given device is judged that it does not have its own efficacy, effectiveness and/or performance as to be concerned in the application.

(b) The given device is judged of no value for medical use because its adverse effect(s) far exceed its efficacy, effectiveness and/or performance.

PMD Act, Article 23-2-5 paragraph (2), item (iii), (a) & (b)
Risk/benefit balance and evidence level are variable by its intended use and claim.

- **Screening**
  - **Performance**: To find few true positive cases in large population.
  - **Risk**: A person loses the opportunity of treatment.

- **Diagnose**
  - **Performance**: To provide diagnosis of true positive and true negative for screened population.
  - **Risk**: A person receives the unnecessary interventions.

- **Treatment**

**Claim**
Claimed to cure disease, change behavior, or else?

How much are false-positive and false-negative rates acceptable? What sort of clinical evidence is needed to support its claim?
Specific Considerations for Artificial Intelligence

**Unpredictability**
Users cannot understand the reasoning of output

- How do you figure out the difficult situation?
  - Expect developing AI technology?, or
  - Run exhaustive situation?

**Plasticity**
Post market learning may be worsen the performance of AI products

- How do you keep the performance of it?
  - Review learning process (how, who, when, what data... etc)
Section 1. Introduction

Issues:

- Algorithm for calculating output is “black box” nature in AI based on deep learning.
- Its performance, especially after post-market training, can only be evaluated by verification of the output.
- How to consider the source or type of the data, authenticity and bias in the learning data?

This guidance summarizes the issues and points to consider on evaluating the efficacy and safety of the medical imaging system for CAD utilizing AI technology in the approval review.
Section 5. Open Problems and direction of their solutions:

(1) Black box
- Approval review process should focus on the performance evaluation by confirming if the input yields the required output.
- Manufacturers should guarantee the performance by indicating that the systems always meet the specifications on performance.
- Functions that inform any unexpected outputs of the system to the users should be also required.

(2) Changes in performance
1. Continuous verification of performance:
   - The assistance systems should be validated every time when their performance changes to ensure their quality, safety, and efficacy.
2. Quality assurance associated with performance changes:
   - Training algorithm and training data should be clarified.
3. Principles on post-market approval process:
   - Necessity of taking the approval process should be determined in accordance with the magnitude of the associated changes in performance and risks.
Section 5. Open Problems and direction of their solutions:  
(3) Assigning responsibility
- Manufacturers are responsible for the maintenance and troubleshooting of systems, and clarifying the use method of the system including by training for users
- Referring to the MHLW Health Policy Bureau notification that medical doctors are responsible for the final decision in diagnosis and treatment

Further technical considerations on the development and evaluation are discussed in Section 6. Points to consider in evaluation.

The potential type of AI for which users can perform post-market training to change their performance is discussed in Annex.

English translation is available on the NIHS website (bottom of the page): http://dmd.nihs.go.jp/jisedai/tsuuchi/index.html
Legal Amendment for medical devices using AI (1)

*Revision of Pharmaceutical and Medical Device Act is currently under discussion in the Diet.

Post-Approval Change Management Protocol will be introduced for medical devices including with AI to make continuous improvement possible.

Current Process

Clinical data collection → Application → Approval

Approval application should be done after collecting necessary data.

New Process

Clinical data collection → Application → Approval

Request or submit of change

Early realization of improvement

Objects for submit
- Change of sizes, components, performances
- Improvement of diagnostic accuracy by using post-marketing RWD
Approval review process which enables continuous improvement of performance of SaMD using AI will be introduced.

- 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 minor change notification, which does not require approval process.

*Compliance is checked in the audit.

*Revision of Pharmaceutical and Medical Device Act is currently under discussion in the Diet.

“Improvement Process” is developed and reviewed in the approval review process.
The situation in Japan:

1. There are some specific consideration in the definitions and review principles of AI devices.

2. Evaluation guidance summarizes the issues and points to consider on evaluating AI devices.

3. Approval review process for AI device will be introduced by the legal amendment proposed.