



Perspectives and Regulatory Considerations for AI based Medical Devices

2019. 11.



Ministry of Food and
Drug Safety





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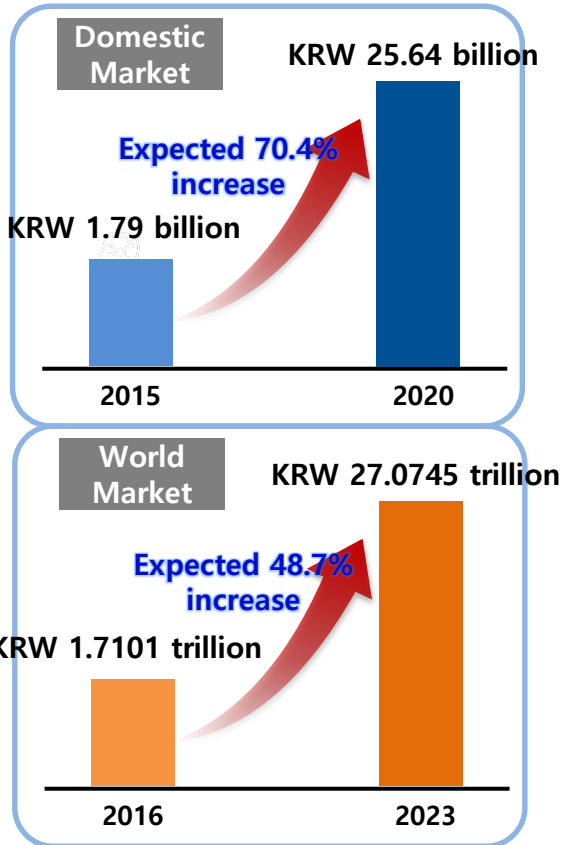
- I** Artificial Intelligence Medical Device Policy
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I . Artificial Intelligence Medical Device Policy Environment and Domestic Approval Status

Artificial Intelligence (AI) Medical Device Policy Environment and Domestic and International Conditions

Outlook on the rapid expansion of the AI-based medical market



* Source Data: Health Industry Brief, Korea Health Industry Development Institute (December 2018)

Allied Market Research (2018), Korea Information Technology Research Institute (2016)

Deregulation of AI-based medical device for rapid market entry

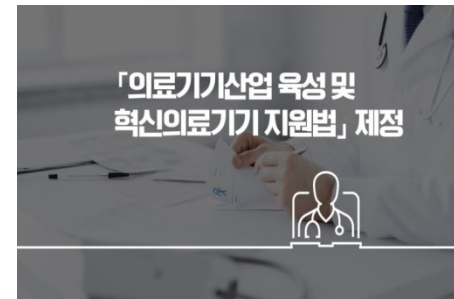
- ✓ Approval/review guidelines with the application of big data and AI technology

(Published on 2017. 11. 22)


- ✓ Guidelines for the evaluation of the clinical efficacy of the AI-based medical device

(Published on 2017. 12. 20)

- ✓ Enactment of 「Medical device industry development and innovation medical device support act」 (Enactment on 2019. 4. 30, Effective from 2020. 5. 1)



AI-Based Medical Device (SW) Approval and Clinical Status

 Clinical Study Protocol Approval Status:
20 cases (7 completed approvals, 13 in progress)

Intended Use

- ✓ Classification of causes of cerebral infarction
- ✓ Breast cancer diagnosis
- ✓ Prostate cancer diagnosis
- ✓ Detection of retinal abnormality, etc.

 Manufacture Approval Status: 8 cases

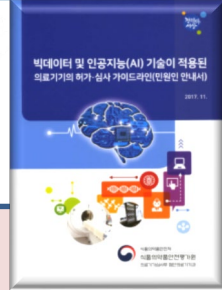
Intended Use

- ✓ Classification of causes of cerebral infarction
- ✓ Detection of pulmonary nodule abnormality
- ✓ Analysis of bone age
- ✓ Detection of lumbar compression fracture abnormality, etc.



II. Policy Enforcement Status

AI-Based Medical Device Guidelines



Guideline on Approval Review of AI and Big Data based Medical Devices (Nov. 2017)

'AI-based medical device'

Definition

It is a medical device in the **form of software** that **diagnoses or predicts disease** by analyzing the **medical information (e.g., medical imaging, medical signals, genetic information, etc.)** through **AI technology** developed to **learn, infer, sense, and understand like humans**.

Subject

- **It is a software** that **automatically diagnoses, predicts, and monitors the possibility of disease or conditions** in a specific patient.
- It is a software that **provides clinical information necessary for diagnosis** by analyzing the medical imaging, **analysis information** from in vitro diagnostic devices, and **patterns or signals** from signal acquisition systems (e.g., electrocardiography)

classification

According to the 「Regulations on Medical Device Items and Classification by Item」

- The main items are classified into **medical imaging analysis device software [2], Computer aided detection software [2], Computer aided diagnosis software [3], and Radiation treatment planning software [2]**.
- **This pertains to four items**, including in vitro diagnostic software items such as **disease prognosis and predictive screening software [2], and cancer prognosis and predictive screening software [3]**.

AI-Based Medical Device Guidelines

Guideline on Approval Review of AI and Big Data based Medical Devices (Nov. 2017)

Approval Review Measures

1. 'Performance' recording method

It describes **technical specifications**, such as **main functions**, cloud server operating environment and service types, and **security standards**.

2. Performance and clinical efficacy validation items

It is the validation of the **accuracy of product diagnostics** with sensitivity, specificity, positive predictive value, negative predictive value, ROC Curve, AUC, etc.

3. Clinical efficacy validation

Depending on the nature of the product, appropriate study method among **prospective study and retrospective study**, or a combination of the two methods can be designed.

4. Scope of data submission

The data on the principle of action must **include diagnostic algorithms** (e.g., machine learnings), and **principles and descriptions on cloud computer technology**.

5. Subject for amendment approval and certification

If the **accuracy is improved by adding learning data** without changing the designs, **procedures shall be exempted**. However, it must be managed under the GMP system.

6. Version management

Parts that **manage the structure and design of products**, and **parts that manage the addition of learning data** by the manufacturer are identified and managed accordingly.

7. Management of learning data

The manufacturer needs to **establish a management policy for learning data** and **update period** for learning data.

8. Approval scope for applying cloud computing technology

When applying cloud computing technology, **cloud service type and server operating environment must be documented**.

※ Please see the next slide for the 'Scope of data submission'.

AI-Based Medical Device Guidelines

Guideline on Clinical Validation of AI based Medical Devices (Dec. 2017)

In order to rationally evaluate clinical efficacy of AI-based medical device (software), **retrospective clinical trials** should be introduced and **present considerations for clinical efficacy evaluation, including the selection of subject data, study method, and efficacy evaluation standard and method.**

Selection of subject data

- **How to select subject data and the number of data**
- After establishing the appropriate statistical hypothesis on **clinical data collected for the clinical trial**, calculate **the number by applying the subject data calculation formula.**
- **Subject Consent: Waiver of subject consent may be considered** based on the approval of the Institutional Review Board (IRB).

Study method

- The study method includes securing the **reference standard**, **study design**, multicenter study, randomization, and blinding, selection of control group and medical device for control study, and **clinician consensus determination.**

Efficacy evaluation standard and method

- **Selection of Endpoints:** The **sensitivity, specificity, ROC curve, AUC**, etc., of the diagnosis are calculated by using the **reference standard.** If no reference standard is available, **concordance rate, etc., should be calculated.** **Success Criteria for Evaluation Results:** The success criteria for the evaluation results of the clinical study may be set **autonomously by the manufacturer**, and **the reasons and basis must be presented.**



Ⅲ. Future Policy Direction

Background

Status of AI-based medical device relevant regulation

- ✓ In the medical field, it is easy to **secure large scale medical big data** due to increase of ICT convergence medical device and **increased development of medical devices with AI technology** → Increased medical device approvals

- ✓ When conducting the approval process of an AI-based medical device (independent software type), **challenges arise during the review progress due to a gap between the company and the reviewer as there is no standard for a comparison method.**

Recognize the need to improve regulations

Flexible regulations are required to respond reasonably to the development of innovative medical technology, which is rapidly changing.

Equivalence Review Status

e.g.,) Comparison of equivalence with the predicated product

For general medical devices

- ✓ **Item Name:** Defibrillator (3)
- ✓ **Purpose of Use**
The device is used to remove atrial or ventricular fibrillation by sending an electric shock to the heart either directly or through an electrode placed on the chest wall with a maximum electrical output within 360J at 50Ω test load.
- ✓ **Principle of Action**
The heart rhythm is analyzed through the electrodes attached to the chest wall with an equipment that has less OOI of output, then if defibrillation is required, send electric shock to the heart to restore normal heart rhythm and resuscitate the patient.

When comparing with the product, it is considered to be **equivalent** if it falls within the category described in the purpose of use, performance, test standard, and method of use.

For independent software

(This is applicable to an AI medical device which is an independent software.)

- ✓ **Item Name:** Computer aided diagnosis software (3)
- ✓ **Purpose of Use**
This is a software used to support the diagnostic decision of medical professionals by presenting the disease, severity of disease, and degree of likelihood of the disease from the medical imaging.
- ✓ **Principle of Action**
The diagnosis algorithm is indicated in the manner of deep learning method.

When comparing with the product, **it is difficult to determine what level would be considered as equivalent in** algorithm, coding, etc.

Medical Devices Industry Development and Innovative Medical Device Support Act (Effective from 1 May 2020)

Highlights of 'Medical Device Software' of the Innovative Medical Device Act

Certification of Innovative Medical Device Companies

Definition

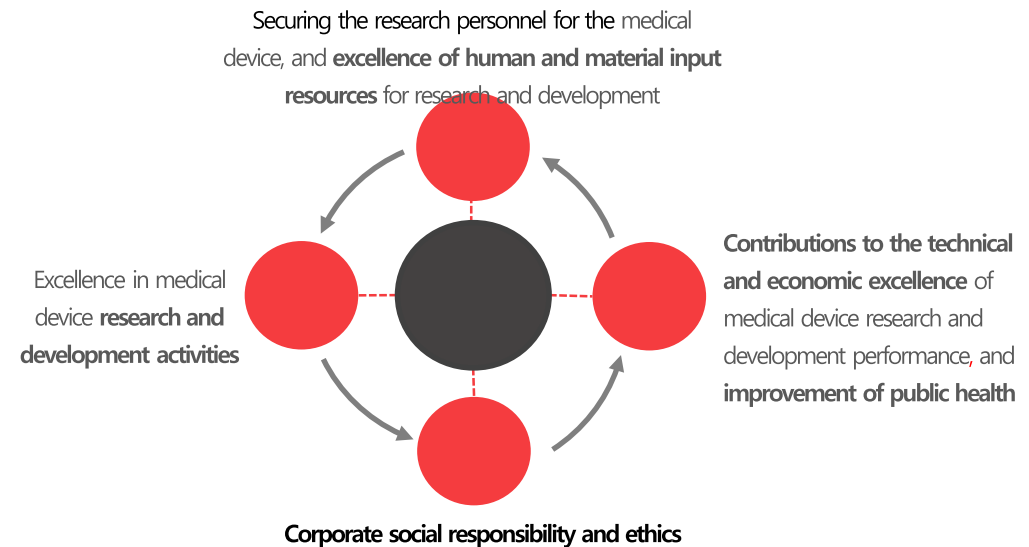
Innovative Medical Device

- **This is the application of cutting-edge technology** in fields of high technology intensity and rapid innovation, such as information and communication technology, biotech and robot technology; or
- **Medical devices that have significantly improved or are expected to improve the safety and efficacy** as compared to the existing medical device or treatments.

Innovative Medical Device Company: This is a **medical device company certified by the Minister of Health and Welfare** – one of the following companies.

- **Medical device companies that have invested more than the scale** prescribed by the Presidential Decree for **research and development of medical devices**
- **Foreign-invested medical device companies with research and development investment record and or currently conducting research and development of medical device**
- **Medical device companies that research, develop, and produce the innovative medical device designated pursuant to Article of this Act**

Considerations for certification of innovative medical device companies



- ※ The application should be submitted directly to the Ministry of Health and Welfare. Certification will be given after the review.
- ※ Re-evaluation will be conducted every 3 years after the certification.

Highlights of “Medical Device Software” of the Innovative Medical Device Act

Special Cases of Innovative Medical Device Software Approval

Introduction of the medical device software manufacturer certification system

- According to the application of a person who plans to manufacture medical device software designated as an innovative medical device, the personnel of the organization and product development standard should be evaluated. If the result of the evaluation is superior, they will be **certified as a medical device software manufacturer**.

☞ Waive a part of data required for manufacturing approval or manufacturing certification

Introduction of the amendment approval system

- **Only critical changes should undergo the amendment approval (certification) process.** ☞ Purpose of use, principle of action, changes in major function, etc.

Pushing forward the waiver of MFDS approval of clinical trial protocol

- **Clinical trial** on medical device software designated as innovative medical devices **should be approved by the IRB**, and this can be regarded as to be **approved by the Minister of Food and Drug Safety**.

Establishing standards for medical device software manufacturing and quality control

- In accordance with the Prime Minister’s Decree of the Act, **obtaining review after being equipped with facilities and manufacturing and quality control system** will be regarded as to be reviewed under the 「Medical Device Act」 Article 6 Subparagraph 4.

Thank you.



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