Taiwan Food and Drug Administration

Guidance for Industry to Register Artificial Intelligence / Machine Learning - Based Software as Medical Device (AI/ML-Based SaMD)

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The English translation is for reference only.
The Chinese version shall still prevail in actuality.

Introduction

To ensure the safety, performance, and quality of software as medical device (SaMD) using artificial intelligence/machine learning (AI/ML) technology, the Taiwan Food and Drug Administration has referred to the regulatory standards of the United States, Japan, Korea, and other countries, as well as International Medical Device Regulatory Forum (IMDRF) documents, to develop this guidance for the manufacturers to evaluate and register their products.

The SaMD with AI/ML technology should comply with the Medical Devices Act and other relevant regulations. The product description, safety and efficacy verification described in this guidance are based on the current literatures. In order to ensure public health and safety, when those products with AI/ML technology applying registration and market approval, the reviewers may request the manufacturers to provide safety and efficacy verification and evaluation information in addition to the items listed in this guidance because the rapid development of science and technology. This guidance will be updated aperiodically.

I. Scope

The term “Artificial Intelligence / Machine Learning-Based Software as Medical Device (AI/ML-Based SaMD)” in this guidance refers to SaMD that uses clinical data (including measurement data, databases, and images) as a source to adapt its performance by simulating human inference or autonomous learning through human-designed software learning models or training methods.

This guidance describes the application of registration and market approval requirements for AI/ML-based SaMD and also applicable to medical devices that use those technology for part of their functions. Concerning the scope of SaMD management and classification principles, please refer to the “Guidance for Classification of Software as Medical Device” and “Regulations Governing the

Classification of Medical Devices".

II. Terms and Definitions

(1) Artificial Intelligence/Machine Learning (AI/ML):

Through scientific knowledge and engineering techniques, machines or computer programs can simulate intelligent human behaviors, such as "voice conversion, visual recognition, motor control, comprehension and learning, reasoning and decision-making, and self-correction".

Machine learning is a subset of artificial intelligence. Through the design of algorithms and data training, computers (software) can learn autonomously from data without excessive programming and improve algorithms through training experience to simulate various computational methods of human learning functions, such as regression analysis, support vector machine, decision tree, and neural networks.

(2) Deep learning (DL):

It is a branch of ML that uses neural network structures (e.g., multilayer neural networks and convolutional neural networks), along with considerable training data, to learn features from these data.

III. Software Overview and Algorithm Framework

(1) Software Overview

Applications for the registration of SaMD for AI/ML technology should include a description of the software functionality and architecture and whether the software is designed with an adaptive or locked algorithm. The medical device firms should provide target functional values (e.g., detection rate, false-positive rate, false-negative rate, testing time, and other necessary factors) based on the product's intended use, effectiveness, indications, contraindications, and limitations of use to ensure performance specifications in the system architecture.

The following are possible product types:

1. **Computer Assisted Detection (CADe):**
   It can automatically extract suspicious lesions from images, mark their location by using AI/ML technology, analyze medical images and other medical test results to aid in the detection of lesions or abnormal values.
2. **Computer Aided Diagnosis (CADx):**
   It can automatically extract suspicious lesions from images and present their values or shapes as quantitative data through AI/ML techniques,

providing diagnostic options and risk assessment results.

3. **Computer Aided Triage:**
   Rapid screening for specific symptoms to help medical staff to reduce or eliminate requirements for the same clinical procedure (e.g., screening patients with acute cerebral hemorrhage).

(2) Algorithm Framework

Applications for SaMD with AI/ML technology should include a description of the algorithm architecture and the corresponding theoretical basis. The product description and specification document must specify the testing principle and algorithm structure. If the product uses ML, DL, or other algorithms with black-box characteristics, the design (modeling) and training method for the algorithm must be described. For example:

1. **Design (modeling)**
   An overview of the original network architecture and software procedures of the SaMD with AI/ML technology used for detection/diagnosis should be provided for the product review.
2. **Training method**
   The applications should clearly state the intended use of the product and define the performance and effectiveness of the auxiliary system. The manufacturers should describe and explain, individually, the data sources, learning methods, validation data, test data, and other necessary factors for the product according to data usage (e.g., training, validation, testing, and updating).
3. **Detection principle and algorithm framework**
   The applications should describe the architecture of the software's algorithms, such as ML and DL.

IV. Data Restrictions of AI/ML Algorithms

The performance of SaMD with AI/ML technology depends on well-designed training methods and considerable appropriate data. To verify the intended use, safety, and performance of the software, the training methods, architecture, procedures, and details such as relevant properties of the data used and measures for maintaining quality should be clearly described.

Because the training methods of AI/ML technology must rely on the analysis of considerable data, the training results are susceptible to the properties and qualities of

the data used. Hence, the methods of acquiring data and maintaining their quality must also be explained.

The data for AI/ML can be divided into training, validation, and testing data. Among these, the testing data must be strictly separated from the other two types of data to avoid bias in validation results. However, correspondence with the declared and intended use of the AI module and its clinical significance must be considered regardless of the data type.

(1) Training Method, Architecture, and Procedure Descriptions

The methods, architecture, and procedures for training an AI module should be explained, including the basic model used, adjustment parts, and pretraining content.

(2) Data

The data used for training the AI module should be described, including patient ethnicity and the clinical significance of the data, form of production materials, production method, and any other additional information.

1. **Ethnicity and Clinical Significance**
   The source and properties of the data, as well as the sampling bias in terms of patient ethnicity and the clinical significance of the data themselves, must be considered.
2. **Production Form**
   This refers to the medical devices or clinical methods that are used to generate data, such as CT, MRI, ultrasound, optical impression, specimen slide images, fluorescent staining images, and physiological parameters.
3. **Production Method**
   This encompasses the process of data production, including the model of instrument used, data acquisition parameters, and data format.
4. **Other Additional Information**
   This information includes additional annotations and the clinical judgments for data and methods for generating these annotations and judgments (e.g., lesion location, size, benign or malignant status, or other diagnostic information).

V. Use Environment and Information Security

(1) Environmental and Personnel Restrictions

The applications for the registration of SaMD with AI/ML technology should include its clinical-use environment restrictions (including software use environment, matching use equipment, software and hardware specifications, and

acquisition parameter settings) and personnel restrictions (such as training and assessment requirements for product use).

(2) Information Security

The SaMD with AI/ML technology that can be connected to a network, with wireless transmission, or is applied to medical mobile application can refer to the "Guidance for Industry on Management of Cybersecurity in Medical Devices" issued by Taiwan Food and Drug Administration, and the documents related to medical device cybersecurity should be provided.

VI. Functional Verification

The software validation reports are required for SaMD with AI/ML technology; please refer to the "Guidance for Validation of Software as Medical Devices" issued by Taiwan Food and Drug Administration. The key points include the following:

1. Level of concern
2. Software description
3. Device hazard analysis
4. Software requirement specifications
5. Architectural design chart
6. Software design specifications
7. Traceability analysis
8. Software development environment description
9. Verification and validation documentation
10. Revision level history
11. Unresolved anomalies, bugs, or defects

Output Results and Judgments

In addition to the aforementioned software validation report, the manner in which the software output results are presented and the reference for the output results of the SaMD with AI/ML technology should be stated.

The software output results must be consistent with the intended use of the product. It is recommended that the following should be included:

1. The manners in which the software output results are presented, such as image marking, segmentation results, morbidity risk estimation, and counting.
2. The limitations of the software output results (e.g., false negatives or false positives and other reasons for misjudgment, such as "the output result of this device alone cannot be used for clinical diagnosis, and whether a patient has a disease must be determined by integrating other clinical tests and evaluations").

3. The subsequent clinical decision-making suggestions based on the software output results (e.g., to seek assistance from professional medical personnel).

VII. Clinical Performance Verification

In general, the performance (e.g., sensitivity, specificity, and accuracy) of SaMD with AI/ML technology is related to the source of clinical data (such as medical image acquisition devices). Hence, the product design specification must define the detailed specifications of applicable or compatible devices (hardware and software).

The specifications of devices claimed to be suitable for use with the product shall be the same as those of the device used for the training data (learning data) for the design and development phase and for the testing data in the performance verification phase. If the specifications of the device claimed to be suitable for use with the product exceed those of the device used for the original product design, development, and performance verification phases, scientific evidence of the specification applicability shall be provided.

In addition, the AI/ML-based SaMD should indicate the basis for reference or comparison of output results (e.g., adoption of clinical standards or comparison with current clinical approaches or clinical practices, such as physician empirical diagnosis and standards published by international authorities).

The following key points are suggested for the manufacturers when drafting study protocols for clinical performance verification:

1. Product claims and intended use
2. Study objectives
3. Patient population (e.g., age and ethnicity)
4. Number of clinicians for performance verification and their qualification
5. Description of the methodology used for gathering clinical information
6. Description of the statistical methods used to analyze the data
7. Study results

VIII. Reference

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2. Regulations Governing the Classification of Medical Devices, Apr.26, 2021.
3. Regulations Governing Issuance of Medical Device License, Listing and Annual Declaration, Apr.29, 2021.
4. Guidance for Classification of Software as Medical Device, TFDA Announcement No. 1091610954, Dec.24, 2020.

5. Guidance for Validation of Software as Medical device, TFDA Announcement No. 1061607211, Dec.15, 2017.
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