Latest updates on CADe/CADx medical device review requirement in Taiwan

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http://www.fda.gov.tw/

OUTLINE

- AI/ML-based medical device regulatory updates.
- Review requirements for AI/ML CADe/x medical device.

AI/ML-based Medical Device Regulatory Updates

- Guidance for drafting predetermined change control plans of AI/ML-enabled medical device software(2024.9*)
- FAQs for product registration consultation of AI/ML medical device (2023.10)
- **Guidance for registration of AI/ML CADe/x medical device (2023.9 revised)**
- Guidance for registration of AI/ML CADe/x medical device (2022.8)
- Guidance for registration of AI/ML CADt medical device (2022.2)
- Guidance for registration of AI/ML SaMD (2020.9 / 2021.8 revised)
- Guidance for registration of AI/ML CADe medical device (2021.7)
- FAQs for registration of AI/ML medical devices (2021.5)
- FAQs for registration of advanced medical devices (2020.5)

AI/ML-based Medical Device Regulatory Updates

Go for it !

Medical Device with Safety, Effectiveness, and Quality

Stop

~~**Perfect Medical Device**~~

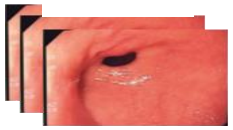
Review requirements for AI/ML CADe/x medical device

Appendix 2, instruction 7

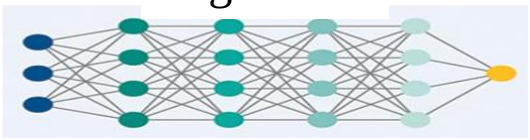
Product Overview

Design &Technical
(Algorithm framework)

Data



Algorithm



Cloud computing

(2) Pre-clinical safety and performance validation

(3) Clinical evidence

(1) Technical Documents

Appendix 2, instruction 9

"Regulations Governing Issuance of Medical Device License, Listing and Annual Declaration" Appendix 2, instruction 8

(1) Technical Documents

Product overview

Refer to “Principles of Compiling Chinese Instructions for Use of Medical Devices” issued by the TFDA for writing the following items:

- Product description
- Intended use, effectiveness, or indications
- Expected foreseeable side effects or complications
- Contraindications
- Warnings, precautions, use restrictions

Algorithm framework

- Algorithm design (modeling) and output functions
- Image/Data processing procedure
- Algorithm training methods
- Reference standard

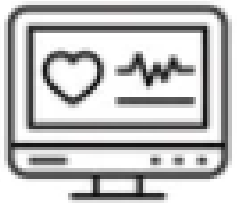
(1) Technical Documents – Product overview

Product overview may include:

- Product name, version, operation system
- Software functionality and architecture
- Adaptive or locked algorithm
- Target functional values (e.g., detection rate, false-positive rate, false-negative rate, testing time, and other necessary factors)
- Precautions, and limitations for use

Possible forms of products：

1. Computer Assisted Detection (CADe)
2. Computer Aided Diagnosis (CADx)
3. Computer Aided Triage and Notification (CADt)
4. Computer-aided acquisition/optimization (CADa/o)

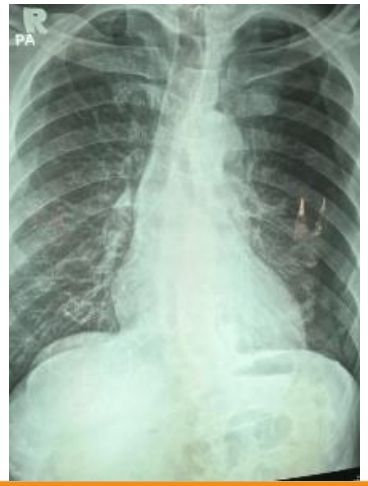


(1) Technical Documents – Algorithm framework

Algorithm framework may include:

- Detail of the algorithm and references
- Input and output data
- Algorithm flowchart
- Calculation processes
- Design and function of each calculation stage
- The specifications of all output marks/parameters

Example: AI-enabled imaging system



- Algorithm design(Modeling) and output function
- Input Image Processing Program
- Algorithm Training Methods
- Reference Standards

(1) Technical Documents – Algorithm framework

e.g., AI-enabled imaging system (1/4)

- **Algorithm design (Modeling) and output function**
  - Algorithm : SVM、CNN、RNN…
  - Development platform: Tensorflow、PyTorch、Caffe…
  - Library : Keras…
  - Model : the number of layers, weights for neural net work…
  - Algorithm function:
    - CADe : The type and meaning of the image marking
    - CADx : Assessment method, quantitative method, the effect and correlation of output result on clinical practice.
  - Algorithm processing flowchart

(1) Technical Documents – Algorithm framework

e.g., AI-enabled imaging system (2/4)

- **Input Image Processing Program**
  - Image processing steps: filtering, segmentation, normalization, registration and correction of artifact or motion.
  - Image normalization calibration-principle and reference basis.

(1) Technical Documents – Algorithm framework

e.g., AI-enabled imaging system (3/4)

Algorithm Training Methods

- Training method, framework, and process
- Training dataset. The dataset employed to train the AI module must be explained:

- Ethnicity and Correspondence with the use：Data source or database, inclusion and exclusion criteria, patient distribution
- Data production form：The type of equipment or clinical practical methods that are used to generate data, such as CT, MRI, PET, ultrasound, endoscopy or others
- Production method：equipment brand and model, data acquisition parameter, data format, image capturing protocol
- Additional information：additional clinical annotations and judgments

(1) Technical Documents – Algorithm framework

e.g., AI-enabled imaging system (4/4)

- **Reference Standards**
  - Ground truth: Output and clinical test results of the same type of device, clinical diagnosis result, biopsy, or doctor's interpretation.
  - If ground truth is doctor's interpretation: Number of doctors, qualification, experience and training requirements
  - If several doctors involve in ground truth decision: The procedure to combined multiple interpretation results to formulate a summarized reference standard.

(2) Safety and performance validation(1/2)

Safety and performance validation

☐ Software validation

-“Guidance for Validation of Medical Device Software”

https://www.fda.gov.tw/TC/siteListContent.aspx?sid=11652&id=36571

☐ Cybersecurity

- “Guidance for Industry on Management of Cybersecurity in Medical Devices” https://www.fda.gov.tw/TC/siteListContent.aspx?sid=11652&id=36818
- “Medical device cybersecurity evaluation templates” https://www.fda.gov.tw/TC/siteListContent.aspx?sid=11652&id=39315

☐ Product claimed functional test

- Output and Detection

(2) Safety and performance validation(2/2)

Software Validation

1. Level of Concern
2. Software Description
3. Device Hazard Analysis
4. Software Requirements Specification, SRS
5. Architecture Design Chart
6. Software Design Specification, SDS
7. Traceability Analysis
8. Software Development Environment Description
9. Verification and Validation Documentation
10. Revision Level History
11. Unresolved Anomalies / Bugs or Defects

https://www.fda.gov.tw/TC/siteListContent.aspx?sid=11652&id=36571

Cybersecurity

- To evaluate safety issues related to wire/wireless functions or data transmission.
- "Guidance for Industry on Management of Cybersecurity in Medical Devices"

Functional Tests

- Conduct test on the product claimed measurement, detection, or output functions and provide the corresponding functional test data
- Safety and functional verification of the product in addition to the Guidance

(3) Clinical evidence information

- Clinical evidence information documents may include:
  - Academic and theoretical bases, relevant research reports and data
  - Clinical evaluation report or clinical trial report
    - → Prospective/Retrospective
    - → Compliance with Good clinical practice (GCP)/ Nonsignificant risk (NSR) clinical investigation

(3) Clinical evidence information

Key considerations during clinical evaluation or clinical trials

- Design specification
- Testing dataset
- Clinical design
- Clinical result analysis methods

(3) Clinical evidence information

Key considerations during clinical evaluation or clinical trials

Design Specification

- Compatible equipment brand and model are required. The model should be identical to the equipment used during the training stage.
- Additional equipment → Additional evidence of compatibility is needed.

Testing dataset

- Data production form and method should be identical to the requirements listed in the instructions.
- Test data should be subgrouped according to clinical-related interfering factors, modifying factors, and comorbidities, and evaluated separately.
- The applicability of the population group.
- If test data is collected from multiple medical institutions, the integration of the data should be explained.

(3) Clinical evidence information

Key considerations during clinical evaluation or clinical trials

Clinical Design

- Actual usage scenarios, the output results, users' professional ability.
- Recommended to use the Multiple Reader Multiple Case (MRMC) method.
- The users (i.e., the readers) should match the intended user population. Qualifications and experience of the readers.
- The method for interpreting clinical results in the clinical design should be consistent with clinical practice.

Clinical result analysis methods

- The primary and secondary assessment criteria for analyzing clinical results should align with the intended use of the product
- Must be confirmed as non-changeable before the start of the clinical evaluation or clinical trial.
- Sensitivity, Specificity, ROC, AUC, Recall rate, False positive rate, etc.

(3) Clinical evidence information

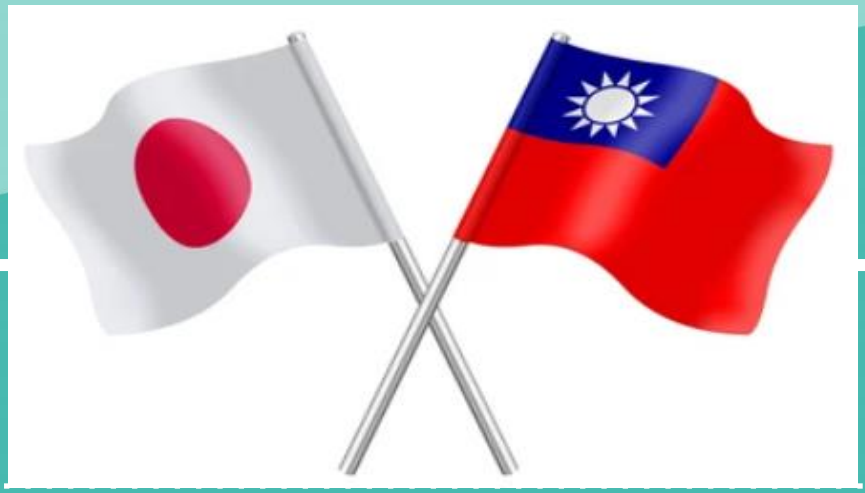
- Contents suggest for inclusion in the clinical evaluation or clinical trial report:
  - Product claims, intended use, and contraindications
  - Study objectives
  - Patient population
  - Number and qualifications of medical personnel participating in the performance assessment
  - Data collection method
  - Statistical analysis method
  - Study results

Special requirements for AI/ML-based CADx medical device

- Possible hazards and corresponding clinical treatment methods in case that AI/ML-based CADx medical device fails, underperforms, or generates false positive or false negative output results.
- Include as many collection sites and data generation device as possible.
- Comparison of conventional diagnosis result and result from the product through statistical analysis.

➢ **Guidance for registration of AI/ML CADe/x medical device (2023.9 revised)**

https://aimd.fda.gov.tw/regulation/detail/42
(Chinese only)



Thank you for your attention

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