RAPS 2022 Convergence

Digital Health/software as a Medical Device/mobile Apps and E-labeling/wearables

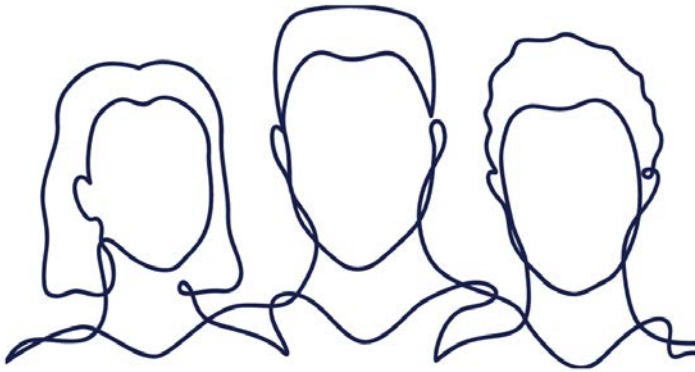
Japan SaMD and AI/ML-enabled Medical Devices regulatory framework

Kuniki Imagawa

Principal Officer

Division of Standards for Medical Devices

Pharmaceuticals and Medical Devices Agency



Medical Devices Regulatory Authorities in Japan

MHLW

Ministry of Health, Labor and Welfare

- Final Authorization of applications
- Publishing Guidelines
- Advisory committee
- Supervising PMDA Activities

PMDA

Pharmaceuticals and Medical Devices Agency

- Scientific Review for Drugs & Medical Devices
- GCP, GMP and QMS Inspection
- Consultation on Clinical Trials, etc.

Legal Structure for Medical Devices

Act	Pharmaceuticals and Medical Devices Act (**PMD Act**), 1960
Cabinet Order	Cabinet Order on PMD Act, 1961
Ministerial Ordinance	Ministerial Ordinance 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.
Notification	Information on application procedures Guidelines for clinical evaluation ,etc.

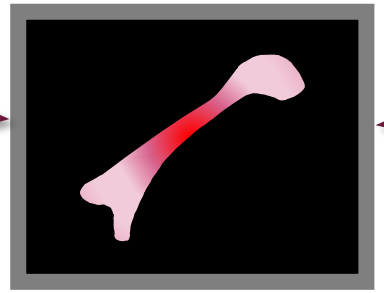
Definition of Medical Devices in PMD Act

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



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

Not intended to diagnose human disease

Intended to diagnose human disease

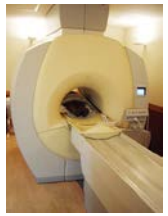
Not MD

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

MD

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

Medical Devices Regulations in Japan

GHTF Classification		PMD Act classification		
		Category	Regulatory requirements	Japanese MD Nomenclature※
Class A	Extremely low risk e.g., X-ray film 	General MDs (Class I)	Self declaration Approval of the product is not required, but marketing notification is necessary.	1,217
Class B	Low risk e.g., MRI, digestive catheters 	Controlled MDs (class II)	Third party Certification Certification by a registered certification body is required. ・Certification Criteria	2,011 (1,518 for 3rd Party)
Class C	Medium risk e.g., dialyzer 	Specially Controlled MDs (class III & IV)	Minister's Approval (Review by PMDA) The Minister's approval for the product is required. ・Approval Criteria ・Review Guideline	815 (43 for 3rd Party)
Class D	High risk e.g., pacemaker 			375

※ JMDN is based on Global Medical Device Nomenclature (GMDN): 2003

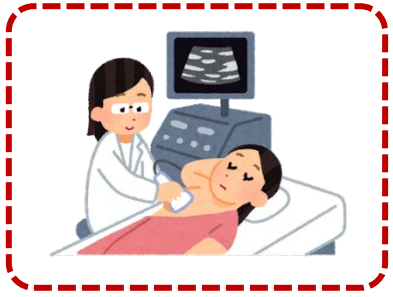
As of 8th Jun. 2022

Transition of regulations for SaMD in Japan

before November 2014

program which determines performance of medical device

install



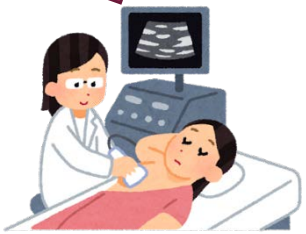
Medical device（tangible object including software）

after November 2014

program which determines performance of medical device

Medical device（software itself）

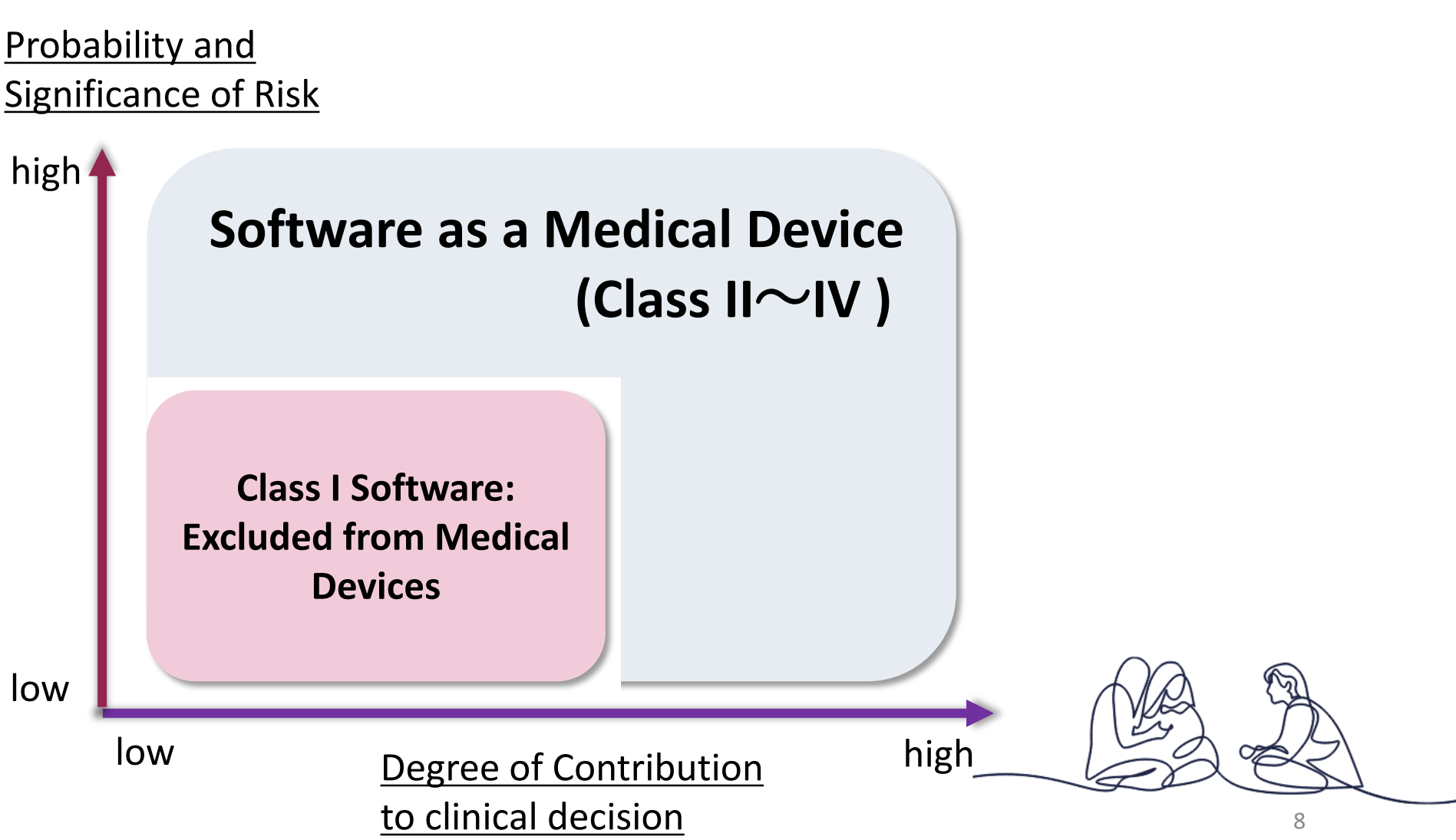
install



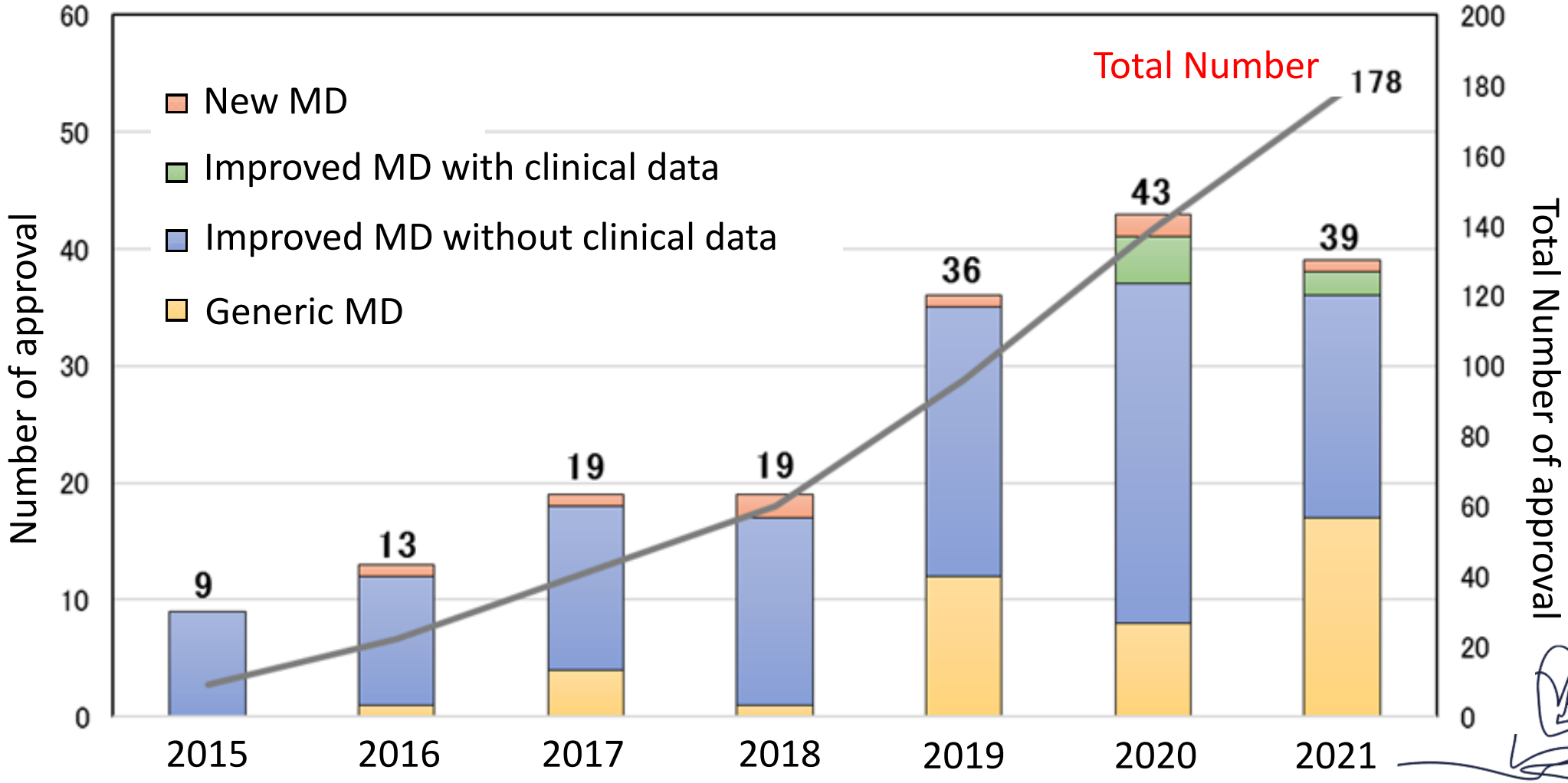
The kind of Software treated as a Medical Device（SaMD）in Japan

Not Medical Device

Not used for prevention, diagnosis or treatment of diseases

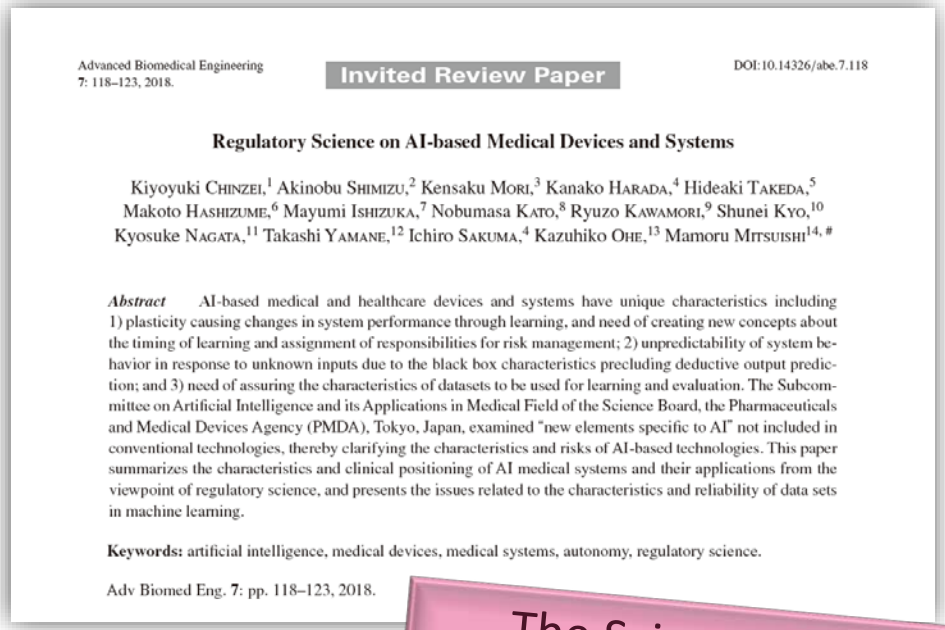


Transition of number of approved SaMD



As of 31st Mar. 2022

Outcome document and Guidance regarding *AI/ML-enabled SaMD*



Advanced Biomedical Engineering
7: 118–123, 2018.

Invited Review Paper

DOI:10.14326/abe.7.118

Regulatory Science on AI-based Medical Devices and Systems

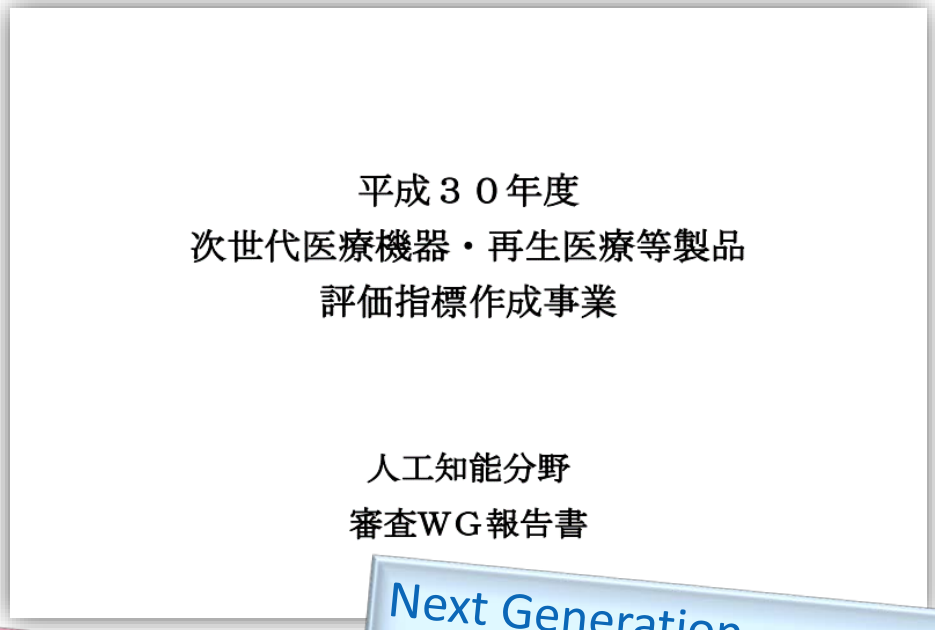
Kiyoyuki CHINZEI,[1] Akinobu SHIMIZU,[2] Kensaku MORI,[3] Kanako HARADA,[4] Hideaki TAKEDA,[5] Makoto HASHIZUME,[6] Mayumi ISHIZUKA,[7] Nobumasa KATO,[8] Ryuzo KAWAMORI,[9] Shunei KYO,[10] Kyosuke NAGATA,[11] Takashi YAMANE,[12] Ichiro SAKUMA,[4] Kazuhiko OHE,[13] Mamoru MITSUISHI[14, #]

Abstract AI-based medical and healthcare devices and systems have unique characteristics including 1) plasticity causing changes in system performance through learning, and need of creating new concepts about the timing of learning and assignment of responsibilities for risk management; 2) unpredictability of system behavior in response to unknown inputs due to the black box characteristics precluding deductive output prediction; and 3) need of assuring the characteristics of datasets to be used for learning and evaluation. The Subcommittee on Artificial Intelligence and its Applications in Medical Field of the Science Board, the Pharmaceuticals and Medical Devices Agency (PMDA), Tokyo, Japan, examined "new elements specific to AI" not included in conventional technologies, thereby clarifying the characteristics and risks of AI-based technologies. This paper summarizes the characteristics and clinical positioning of AI medical systems and their applications from the viewpoint of regulatory science, and presents the issues related to the characteristics and reliability of data sets in machine learning.

Keywords: artificial intelligence, medical devices, medical systems, autonomy, regulatory science.

Adv Biomed Eng. **7**: pp. 118–123, 2018.

The Science Board



平成３０年度
次世代医療機器・再生医療等製品
評価指標作成事業

人工知能分野
審査ＷＧ報告書

Next Generation Evaluation Guidance

English Version;
https://www.jstage.jst.go.jp/article/abe/7/0/7_7_118/_article/-char/en

English Version;
https://dmd.nihs.go.jp/jisedai/tsuuchi/Guidance_for_evaluation_of_AI_assisted_systems.pdf

The example of approval *AI/ML-enabled SaMD* in Japan

Approval data	Medical Device Nomenclature (JMDN)
2018.12.6	Supporting software for differential diagnosis with endoscopic imaging
2019.9.17	Software for MRI system workstation
2019.12.25	Software for general-purpose imaging system workstation
2020.4.27	Supporting software for differential diagnosis with endoscopic imaging
2020.5.8	Software for general-purpose imaging system workstation
2020.6.3	Software for diagnostic X-ray imaging system workstation
2020.6.19	Software for general-purpose imaging system workstation
2020.6.29	Supporting software for detecting lesion with endoscopic imaging
2020.6.29	Software for diagnostic X-ray imaging system workstation
2020.7.15	Supporting software for differential diagnosis with endoscopic imaging
2020.8.20	Software for diagnostic X-ray imaging system workstation
2020.9.2	Supporting software for differential diagnosis with endoscopic imaging
2020.11.24	Software for ultrasound imaging system workstation
2020.11.30	Supporting software for detecting lesion with endoscopic imaging
2021.5.26	Software for general-purpose imaging system workstation
2021.7.7	Software for general-purpose imaging system workstation
2021.9.1	Software for general-purpose imaging system workstation
2021.10.11	Software for diagnostic X-ray imaging system workstation
2021.12.9	Software for general-purpose imaging system workstation
2021.12.24	Software for diagnostic X-ray imaging system workstation
2022.6.2	Software for diagnostic X-ray imaging system workstation

【Approval Product 】

- The majority of them are CAD by using Machine Learning（Locked type）

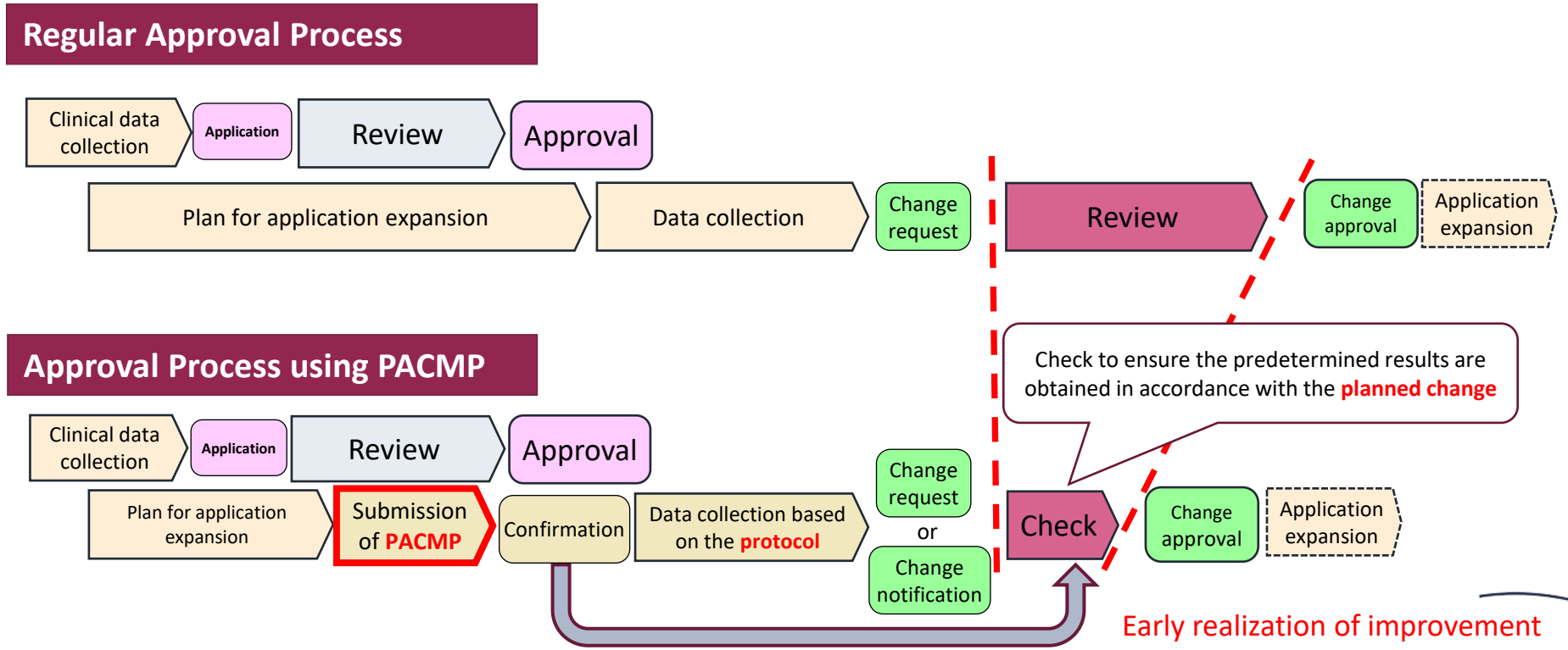
- **Type of Machine Learning;**
  Support Vector Machine, Deep Neural Network, Convolutional Neural Network, Cascade Classifier, etc.

- **Target Disease;**
  Lung nodules, Brain tumor, Breast tumor, Colorectal cancer, Covid-19, etc.

- **Modality;**
  X-ray, CT, MRI, Ultrasound, Endoscopy, etc.

Utilization of Post-Approval Change Management Protocol Challenge to accept “Plasticity” in regulation

Post-Approval Change Management Protocol (PACMP) is introduced for medical devices to enable continuous improvements through product lifecycle.



PMDA Science Board

Universities
Research Institutes

Medical institutions

Collaboration

pmda

- Exchange opinions
- Between top-class researchers in Japan and PMDA reviewers
- Assess cutting-edge technologies

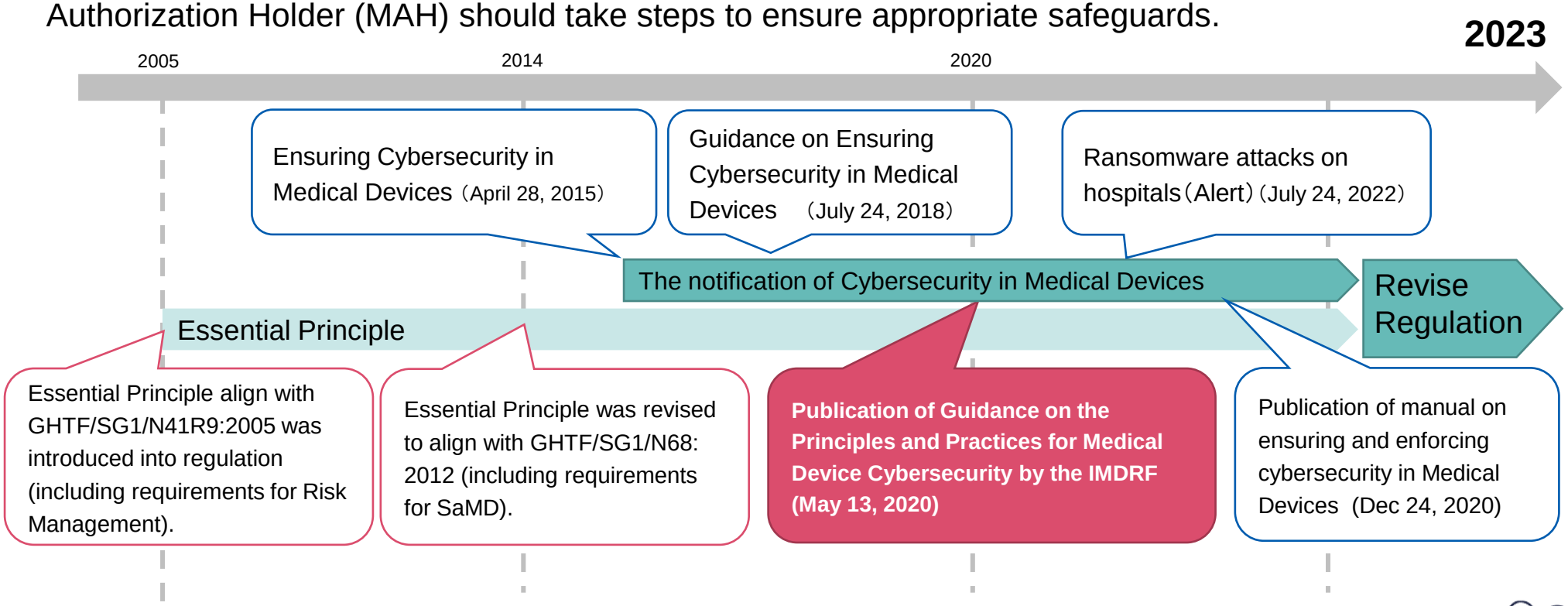
Theme of on Science board in fiscal year 2022

AI/ML-enabled Medical Devices

- Re-use test data such as performance change at post-marketing.
- Comprehensive (various) test data considering intended use and clinical practice.
- How to review for adaptive AI.

Cybersecurity in Japan

The notification regarding Cybersecurity in Medical Devices was published on 2015, and Marketing Authorization Holder (MAH) should take steps to ensure appropriate safeguards.



“Principles and Practices for Medical Device Cybersecurity”（IMDRF/CYBER WG/N60 FINAL:2020）was published on 20 April 2020.

⇒ Japan will introduce this IMDRF documents into regulation by March 2023