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Regulatory Updates on Medical Devices in Japan

- Amendment of the Pharmaceuticals and Medical Devices Act（PMD Act）

-Software as a Medical Device(SaMD)

Hirooki Tanabe

Deputy Director,

Medical Device Evaluation Division,

Ministry of Health, Labour and Welfare, Japan (MHLW)

Legal Structure for Medical Device

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.
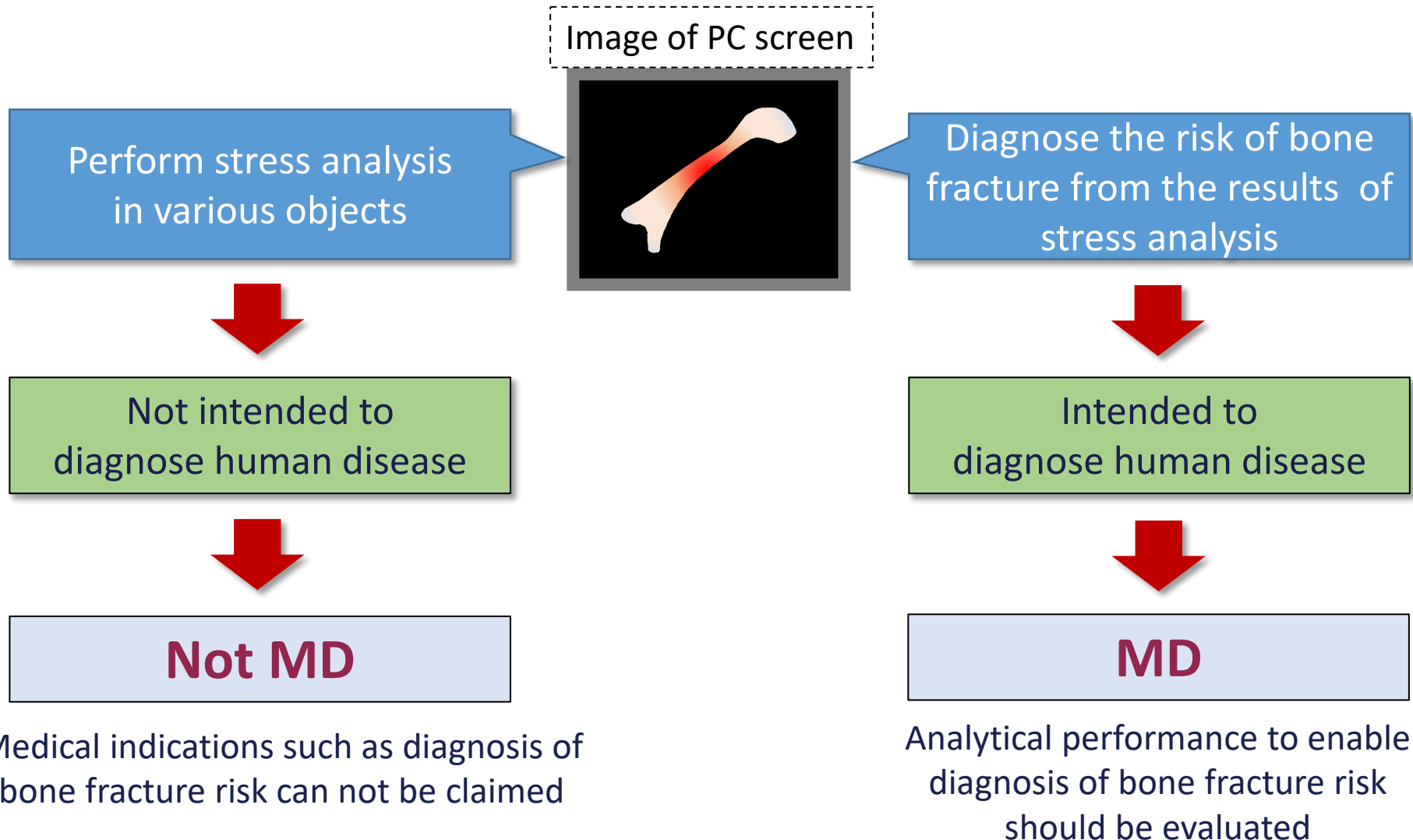
Notification

Information on application procedures
Guidelines for clinical evaluation etc.
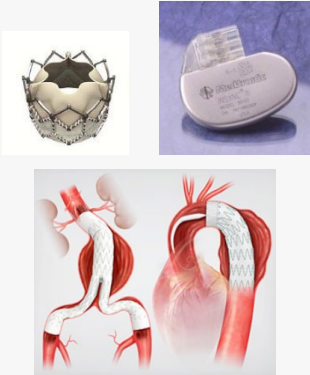
Definition of Medical Device in PMD Act

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

Image of PC screen

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

MD

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

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

Medical Device Regulations in Japan

Classification	Class I	Class II	Class III	Class IV
Category	General MDs	Controlled MDs	Specially controlled MDs	
Premarket regulation	Self-declaration	Third party certification	MHLW approval (PMDA review)	
Example				
Post market safety (vigilance/surveillance)	PMDA and MHLW			

Special Approval for Emergency on Remdesivir

2020 May 2nd

Cabinet Order was amended to expand the scope of Special Approval for Emergency **to include the drugs for novel coronavirus**

Novel Influenza ➕ **COVID-19**

May 4th

Regulatory Submission by Gilead Sciences

PMDA prepared the report for the available information, approval conditions etc..

May 7th **Discussed by Pharmaceutical Affairs and Food Sanitation Council of the MHLW**

Special Approval for Emergency on Remdesivir

https://www.pmda.go.jp/english/int-activities/0004.pdf

Under article 14-3 of the PMD Act, a certain medical product may be approved under when
① an emergency situation requires an unapproved medical product to be used to prevent damage to the public health caused by the spread of diseases
② such emergency situation cannot be managed appropriately by any means other than the use of the unapproved product, and
③ such product is legally available in a country with a regulatory system for medical products that is equivalent to Japan

Amendment of Pharmaceuticals and Medical Devices Act (PMD Act)

Aim

- **to enact a mechanism of early approval**
  conditional, time-limited marketing approval may be granted in emergencies if the efficacy of the pharmaceutical, medical device, or regenerative medicine is estimated and safety is confirmed
- to enact a mechanism of electronic prescriptions

Outline

1. Marketing Approval in Emergencies

New mechanisms to enable early marketing approval in emergencies.

(1) Eligibility of pharmaceutical, etc. to which the early approval is applicable
A pharmaceutical, etc. that needs to be used urgently in order to prevent the spread of a disease or other health hazard that could seriously affect the lives and health of people is eligible for early approval if there is no alternative existing treatment.

(2) Application standards
Assuming that safety has been confirmed, approval may be granted if the efficacy of the pharmaceutical, etc. has been estimated.

(3) Conditions and term of approval
As approval is granted at the early stage where efficacy has been estimated, conditions are provided to ensure the proper use of the pharmaceutical, etc. and restrictions are set in place that limit the duration of the approval to a short term.

(4) Special measures to expedite review process
Special measures are introduced for GMP inspections, national verifications as well as regulations on containers and packaging of the pharmaceutical, etc., in order to expedite review process for approval.

2. Creation of a mechanism for electronic prescriptions

Effective Date

The effective date (1. Marketing Approval in Emergencies): 20 May 2022

厚生労働省 ひと、くらし、みらいのために
Ministry of Health, Labour and Welfare

Transition of regulations for SaMD in Japan

before November 2014

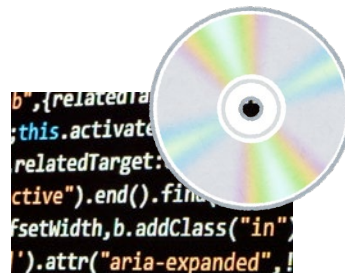program which determines performance of medical device

install

Medical device
（**tangible object including software**）

after November 2014

program which determines performance of medical device
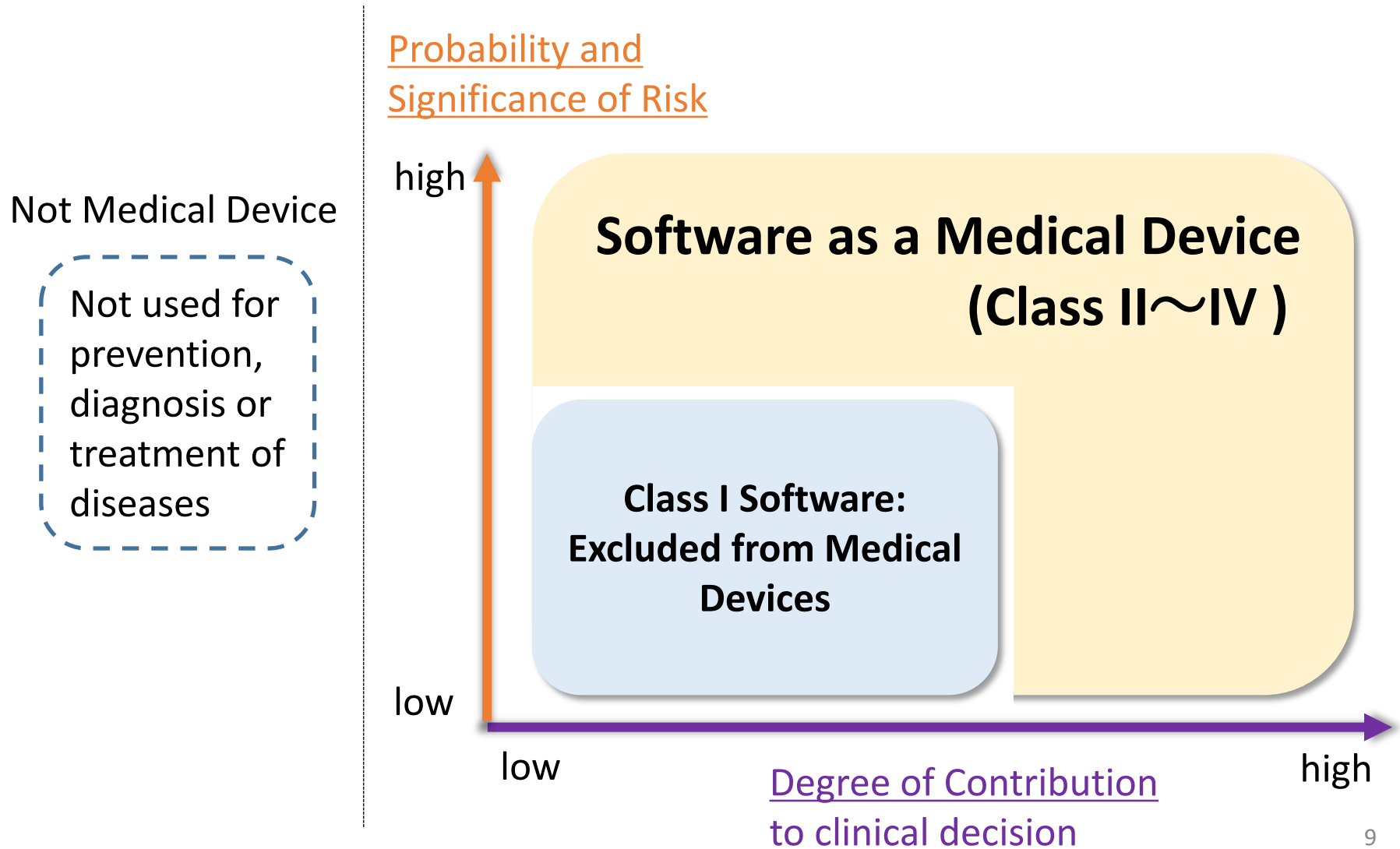
Medical device（**software itself**）

install

MD software classified as Class I is **NOT** subjected to regulations on PMD-Act

The kind of Software treated as a Medical Device in Japan

Not Medical Device

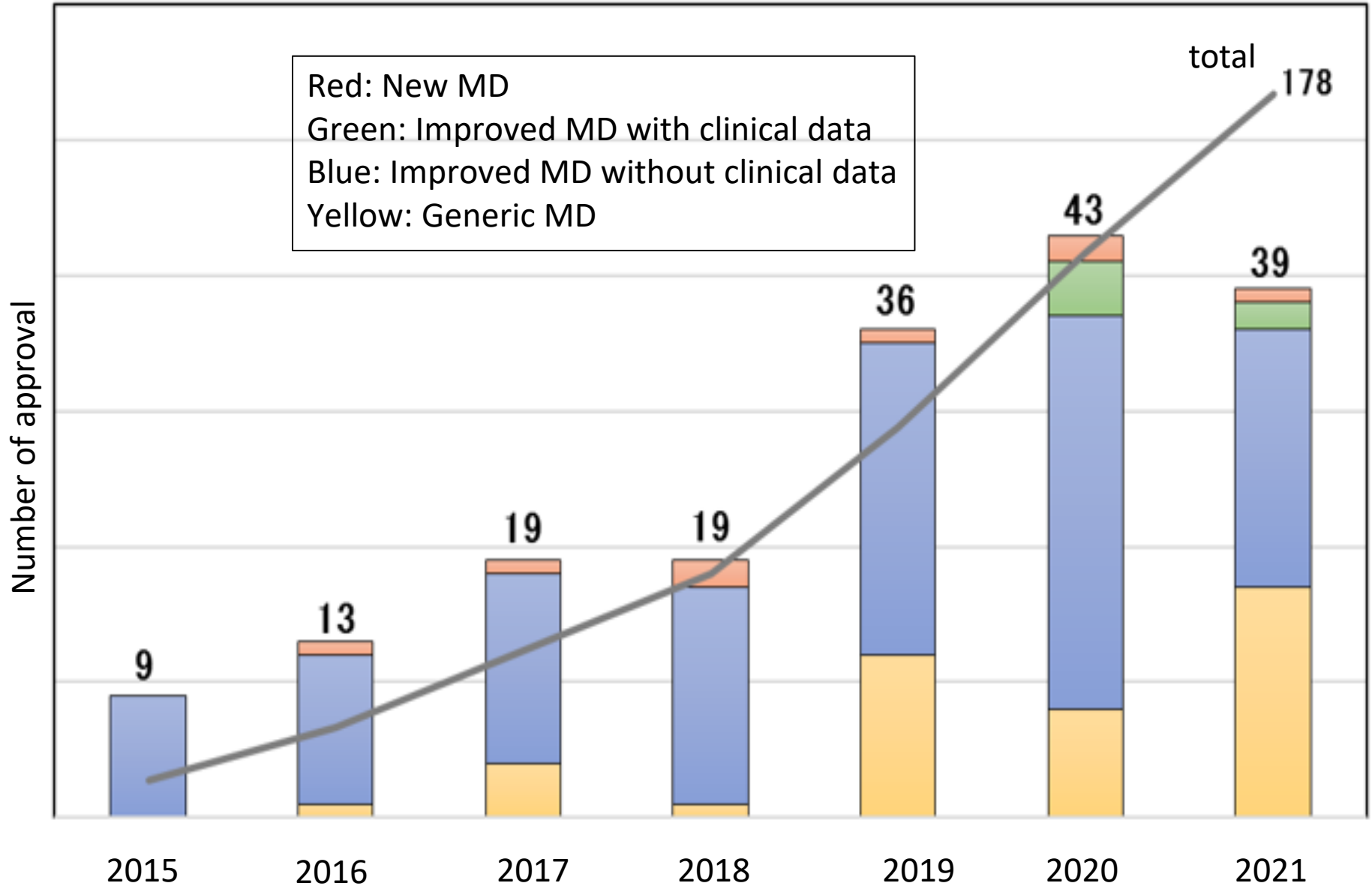Not used for prevention, diagnosis or treatment of diseases

Probability and Significance of Risk

high

Software as a Medical Device (Class II～IV)

Class I Software: Excluded from Medical Devices

low

low

high

Degree of Contribution to clinical decision

Overview of SaMD regulations

Non-medical device	Medical device		
Not for diagnostics or treatment etc. <u>**corresponded to class I**</u>	**Class II**	**Class III**	**Class IV**

For treatment

Programs for personal healthcare
（ex: programs which give advice on meal or exercise for health mentainance and promotion)

Educational program
（ex: training programs for health care professionals）

In-hospital business support program
(ex: medical appointment system, electronic medical record)

Programs corresponded to class I
（ex: eye test, programs for color perception test ）

Program for therapy planning support **61 items**

Application for behavioral therapy **1 item**

Programmer for active implantable device **2 items**

For diagnostics

Program for computer assisted Imaging diagnostics **263 items**

Program for computer assisted diagnostics other than imaging **71 items**

Program for gene mutation analysis **7 items**

Program for diagnostics assist for home use **2items**

as of March 31, 2022

Transition of number of approved SaMD

Red: New MD
Green: Improved MD with clinical data
Blue: Improved MD without clinical data
Yellow: Generic MD

total 178

43

39

36

19   19

13

9

Number of approval

2015   2016   2017   2018   2019   2020   2021

as of March 31, 2022 [11]

Examples of approved SaMD

（Ex.1）
Digital Therapeutic App for Hypertension
（approved on Apr. 2022）
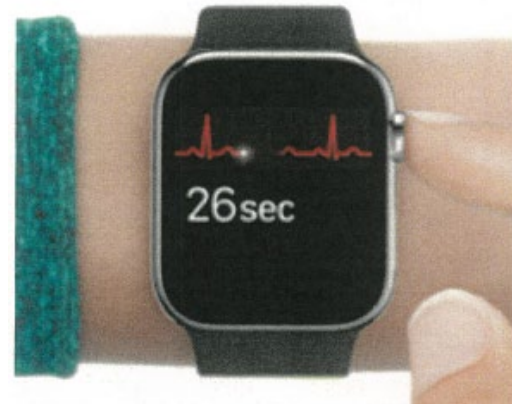
→ Behavioral Approaches to Lifestyle Modification

（Ex.2）
ELECTROCARDIOGRAPH SOFTWARE FOR OVER-THE-COUNTER USE
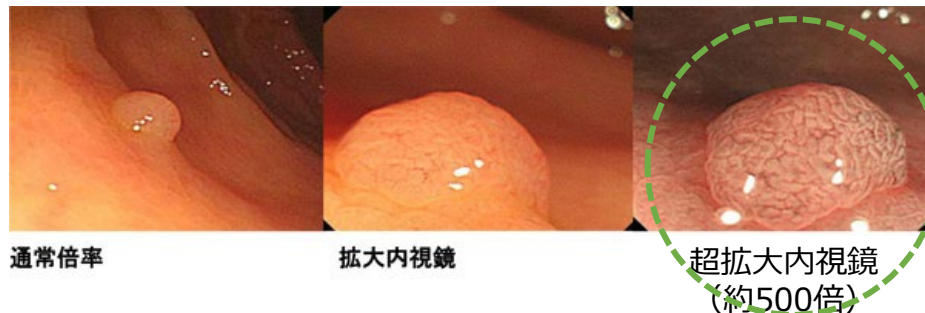（approved on Sep. 2022）

→ can provide information for identifying cardiac arrhythmias and encourage medical examination

（Ex.3）
AI-Equipped Colorectal Endoscopy Diagnosis Support Software
（approved on Dec. 2020）

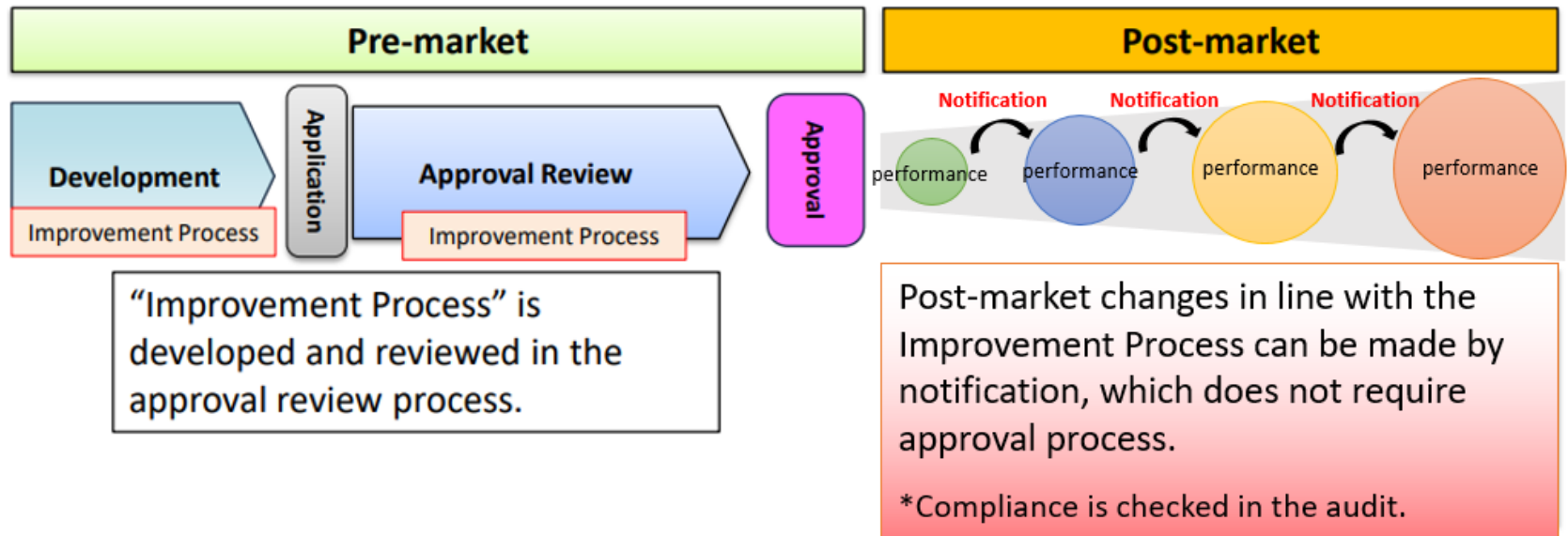→ Support for detection and differentiation of lesions in colonoscopy

通常倍率　　　　　　拡大内視鏡　　　　　　超拡大内視鏡
（約500倍）

Neoplastic: 89 %
Non-neoplastic: 11 %

For polyps/cancers　*Doctor's diagnosis has priority. Please use this output as a reference.

Utilization of Post-Approval Change Management Protocol (PACMP) ～Challenge to accept "Plasticity" in regulation～

Approval review process which enables continuous improvement of performance of SaMD using AI was introduced in September, 2020.

- 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.

Pre-market

Development
Improvement Process

Application

Approval Review
Improvement Process

Approval

Post-market

Notification   Notification   Notification

performance   performance   performance   performance

"Improvement Process" is developed and reviewed in the approval review process.

Post-market changes in line with the Improvement Process can be made by notification, which does not require approval process.

*Compliance is checked in the audit.

"DASH for SaMD"

DX(Digital Transformation) Action Strategies in Healthcare for SaMD (Software as a Medical Device)

1. Early recognition of research seeds and publication of the review guide

a. Assess seeds of technology in the early stage of research.
b. Organize and publish the review guide regarding characteristics of SaMD.

2. Centralization of the consultation contact desk

c. Centralize consultation service (April 1, 2021)
d. Marshal and publish consultation case examples
   https://www.mhlw.go.jp/stf/seisakunitsuite/bunya/0000179749_00004.html

3. Review system applicable to unique characteristics of SaMD

e. Carry out efficient review based on characteristics of SaMD
f. Utilize the Post-Approval Change Management Protocol (PACMP) scheme
g. Consider establishing the innovative SaMD designation program

4. Enhancement of structure for early realization

h. Establish new office specialized in SaMD in MHLW and PMDA (April 1, 2021)
i. Establish Expert Examination Committee for SaMD in the Pharmaceutical Affairs and Food Sanitation Council (April 1, 2021)
j. Establish collaborative forum among regulator, academia and industry
                                                                    (February 4, 2022)
k. Enrich published database of approval cases
   https://www.pmda.go.jp/PmdaSearch/kikiSearch/

Thank you for your attention

MHLW Website
https://www.mhlw.go.jp/english/

PMDA Website
https://www.pmda.go.jp/english/index.html