FDA Perspectives: SaMD, AI/ML and Innovation in Medical Devices

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Overview

- FDA SaMD and AI/ML Overview
- International Medical Device Regulators Forum Working Group Activity
  - AI/ML Working Group
  - SaMD Working Group
- Resources for Industry
- Questions

Quick Show of Hands

- Who here is involved in SaMD development?
- Who here is involved in AI/ML enabled device development?
- Who here thinks SaMD and AI/ML enabled devices are literally the same thing?

It has been almost 10 years since IMDRF defined SaMD

Published in December 2013*, the term "Software as a Medical Device" (SaMD) is defined as software intended to be used for one or more medical purposes that perform these purposes without being part of a hardware medical device.

NOTES:

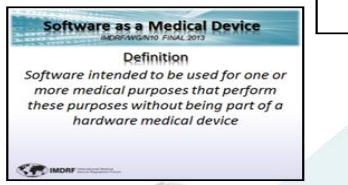
- SaMD is a medical device and includes in-vitro diagnostic (IVD) medical device.
- SaMD is capable of running on general purpose (non-medical purpose) computing platforms
- "without being part of" means software not necessary for a hardware medical device to achieve its intended medical purpose;
- Software does not meet the definition of SaMD if its intended purpose is to drive a hardware medical device.
- SaMD may be used in combination (e.g., as a module) with other products including medical devices;
- SaMD may be interfaced with other medical devices, including hardware medical devices and other SaMD software, as well as general purpose software
- Mobile apps that meet the definition above are considered SaMD.

* *IMDRF/SaMD WG/N10FINAL: 2013: Software as a Medical Device (SaMD): Key Definitions*

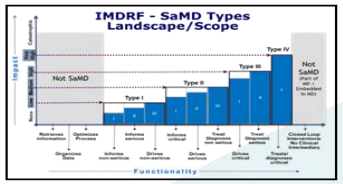
There are 5 key points to remember about SaMD

1. SaMD is a medical device and includes an in-vitro diagnostic (IVD)
2. SaMD can run on general purpose (non-medical purpose) computing platforms without being part of a hardware medical device to achieve its intended medical purpose
3. SaMD can be used in combination with other products including medical devices
4. SaMD can interface with other medical devices, including hardware medical devices, other SaMD software, and general-purpose software
5. Mobile apps that meet the definition above are SaMD

The International Medical Device Regulatory Forum (IMDRF) has issued a series of document related to SaMD

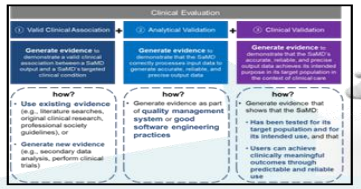


2013
Foundational vocabulary



2014 – Risk framework based on impact to patients

2015 – Quality Management Systems (QMS) control ➔Translating Software development practices to regulatory QMS



2017
SaMD – Clinical Evaluation ➔Generating evidence for clinically meaningful SaMD

Principles and Practices for Software Bill of Materials for Medical Device Cybersecurity
Started July 2022

Additional Work

[Machine Learning-enabled Medical Devices: Key Terms and Definitions]
Published May 2022

[Principles and Practices for Medical Device Cybersecurity]
Published April 2020

It is also important to know when Software is not SaMD

≠ SaMD

Software embedded in a medical device to "drive or control" that device

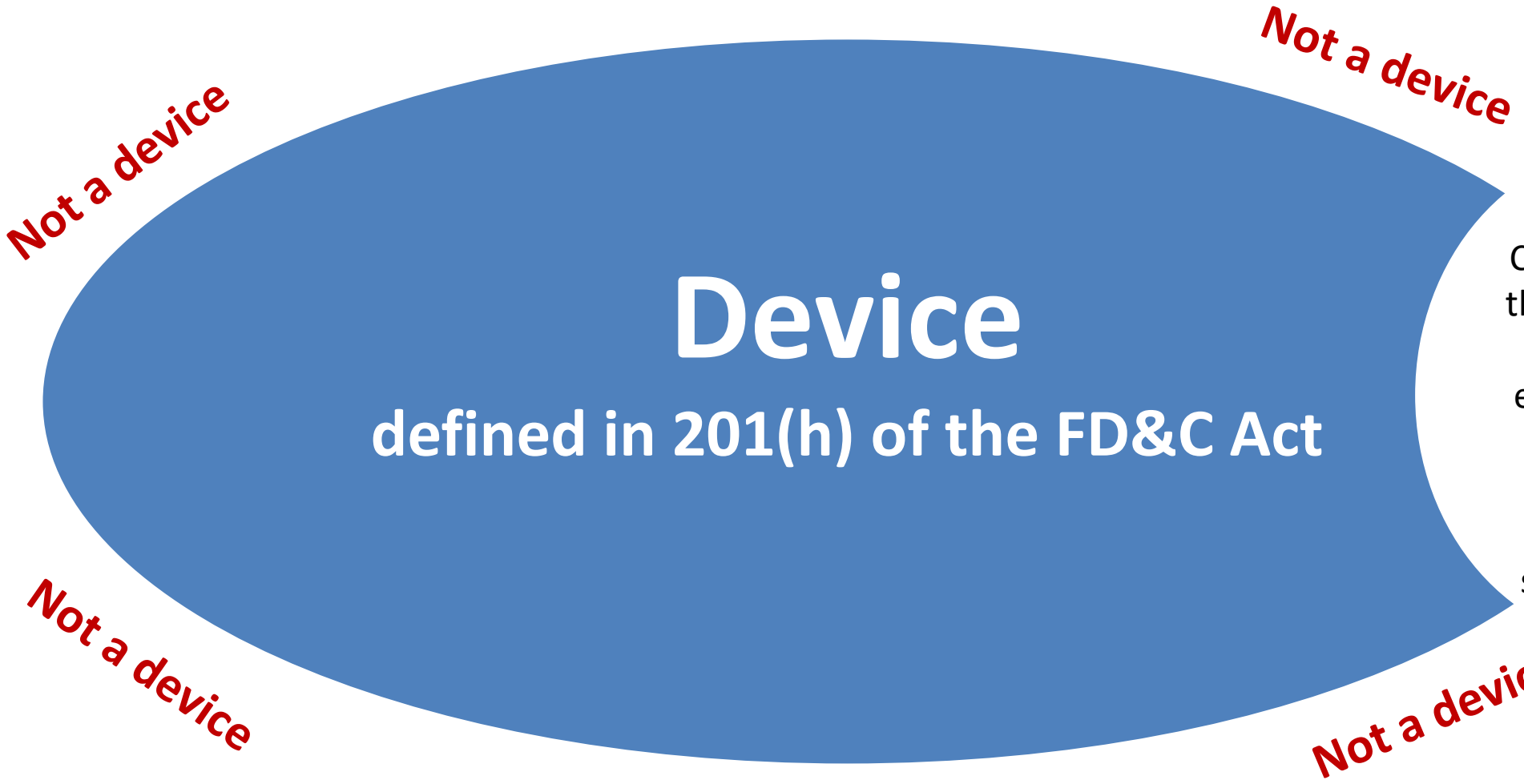
≠ SaMD

Software which is an accessory to a medical device or in vitro diagnostic medical device

Test Your Knowledge

Software that programs MRI magnets to turn	≠ SaMD
Software that helps radiologists and clinicians find and diagnose a cardiovascular condition by analyzing MRI scans	SaMD
Software used in a closed-loop control of a pacemaker	≠ SaMD
Software which retrieves information and performs a further action on that information to inform and/or help (directly or via a clinician) to treat or diagnose	SaMD

The US FDA has harmonized SaMD definition with IMDRF while taking in consideration US legislation



21st Century Cures amended the definition of "device" to exclude certain **software functions** pursuant to section 520(o)

Changes resulting from 21st Century Cures Act helped clarify how to interpret SaMD definition

December 13, 2016, the Cures Act amended the definition of "device" in the Federal Food, Drug, and Cosmetic Act to **exclude certain software functions**, pursuant to section 520(o), intended for...

- **Certain software functions intended for administrative support of a health care facility;**
- **Certain software functions intended for maintaining or encouraging a healthy lifestyle with no reference to any disease or condition;**
- **Certain software functions intended to serve as electronic patient records;**
- **Certain software functions intended for transferring, storing, converting formats, or displaying data and results;**
- **Certain software functions that are intended for clinical decision support.**

Changes to Existing Medical Software Policies Resulting from Section 3060 of the 21st Century Cures Act
https://www.fda.gov/regulatory-information/search-fda-guidance-documents/changes-existing-medical-software-policies-resulting-section-3060-21st-century-cures-act

The U.S. has defined certain terms to help with further clarity

Function	A distinct purpose of a product
Device Function	A function that meets the definition of a device under section 201(h)(1) of the FD&C Act
Device Software Function	Software function that meets the device definition in section 201(h) of the FD&C Act.
Other Function	A function that: – does not meet the definition of a device; – meets the definition of device, but is not subject to premarket review (e.g., 510(k)-exempt); or – meets the definition of device, but for which FDA has expressed its intention not to enforce compliance with applicable regulatory controls.
Device Function-Under-Review	A function for which FDA is conducting a premarket review
Multiple Function Device Product	A product that contains at least one device function and at least one other function.

Function could be the intended use or a subset of the intended use of the product.

Examples

A product with an intended use to analyze data has one function: analysis.

A product with an intended use to store, transfer, and analyze data has three functions: (1) storage, (2) transfer, and (3) analysis.

Despite legislation and attempts to clarify what is, or what is not a SaMD, we still get questions on what is the right regulatory pathway

Examples of Software Function Regulatory Approach

Not a Device

Software functions that are intended for individuals to log, record, track, evaluate, or make decisions or behavioral suggestions related to developing or maintaining general fitness, health or wellness, with no reference to a disease or condition

Intention to Exercise Enforcement Discretion

Software functions that provide periodic educational information, reminders, or motivational guidance to smokers trying to quit, patients recovering from addiction, or pregnant women

Focus of FDA's Oversight

Software functions that use a sensor or lead that is connected to a mobile platform to measure and display the electrical signal produced by the heart (electrocardiograph or ECG)

Increasing Risk

Poised for growth, SaMD promises innovation for providers and patients

Healthy Living	Prevention	Diagnosis	Treatment	Recovery	Home Care	Management

Moving health care from the clinic to the patient

Understanding behavior and physiology in the real world

Leveraging computing power, sensors, connectivity, and software

Wearables: Vital signs monitors ; Sleep Apnea Monitors (PSG); Neurological Monitors; Activity Trackers/ Actigraphy

Software Solutions: Software as a Medical Device (Diagnostic and Therapeutic, CADx, CADe); General Wellness Apps

Tele-care: Activity monitoring; Remote medication management; Video Consultation

Healthcare Analytics: Public Health analytics; Care delivery analytics

Services: Healthcare systems services; Monitoring services for Chronic disease management; Monitoring services for aging; Post acute monitoring

Health and Wellness Solutions

- Improve Cognitive Function
- Promote Exercise & Weight Management
- Stress Management
- Mood and Resilience
- Disability Solutions
- Addressing Isolation
- Grief Counseling

Diagnostics and Therapeutic Solutions Areas:
Post-Traumatic Stress Disorder; Generalized Anxiety Disorder; Depression adjunct therapy; Mild Cognitive Impairment; Autism Spectrum Disorder; ADHD; Neuropsychological Diagnosis and Therapy; Behavioral Therapy

Post Care solution: Activities of Daily Living; Physical Medicine – OT/PT

Patient engagement: routine lab result; appointment reminders; treatment prompts prescription refills; adherence to treatment; Patient Education

The US FDA and the European Commission have issued several public documents to help navigate SaMD

US FDA	European Commission
Policy for Device Software Functions and Mobile Medical Applications	Is your software a medical device?
Medical Device Data Systems, Medical Image Storage Devices, and Medical Image Communications Devices	Guidance on classification of medical devices
Changes to Existing Medical Software Policies Resulting from Section 3060 of the 21st Century Cures Act	Guidance on cybersecurity for medical devices
Use of Electronic Health Record Data in Clinical Investigations Guidance for Industry	Qualification and classification of software

AI/ML-Enabled Medical Devices

Artificial Intelligence (AI):
A branch of computer science, statistics, and engineering that uses algorithms or models to perform tasks and exhibit behaviors such as learning, making decisions and making predictions.

Machine Learning (ML):
A subset of AI that allows computer algorithms to learn through data, without being explicitly programmed, to perform a task.

AI/ML-Enabled Medical Device:
A medical device that uses machine learning to achieve its intended medical purpose.

Descriptions adapted from IMDRF Artificial Intelligence Medical Devices Key Terms & Definitions
Proposed document posted for public consultation Sept 2021 through Nov 29, 2021
http://www.imdrf.org/consultations/cons-aimd-mlmd-ktd.asp

Examples: AI/ML-Enabled Medical Devices

FDA News Release

FDA Authorizes Marketing of First Cardiac Ultrasound Software That Uses Artificial Intelligence to Guide User

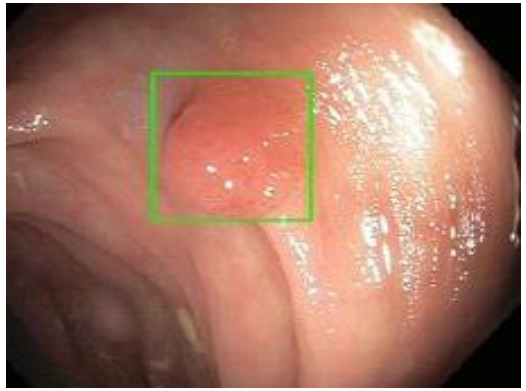
February 7, 2020

Caption Guidance

FDA News Release

FDA Authorizes Marketing of First Device that Uses Artificial Intelligence to Help Detect Potential Signs of Colon Cancer

April 9, 2021



GI Genius

Caption Guidance™ (Caption Health, Brisbane AU). Figure from www.captionhealth.com
GI Genius™ (Medtronic Inc., Minneapolis, Minnesota, USA). Figure from Hassan C et al. Gut. 2019.

AI/ML-Enabled Medical Devices: Opportunities & Challenges

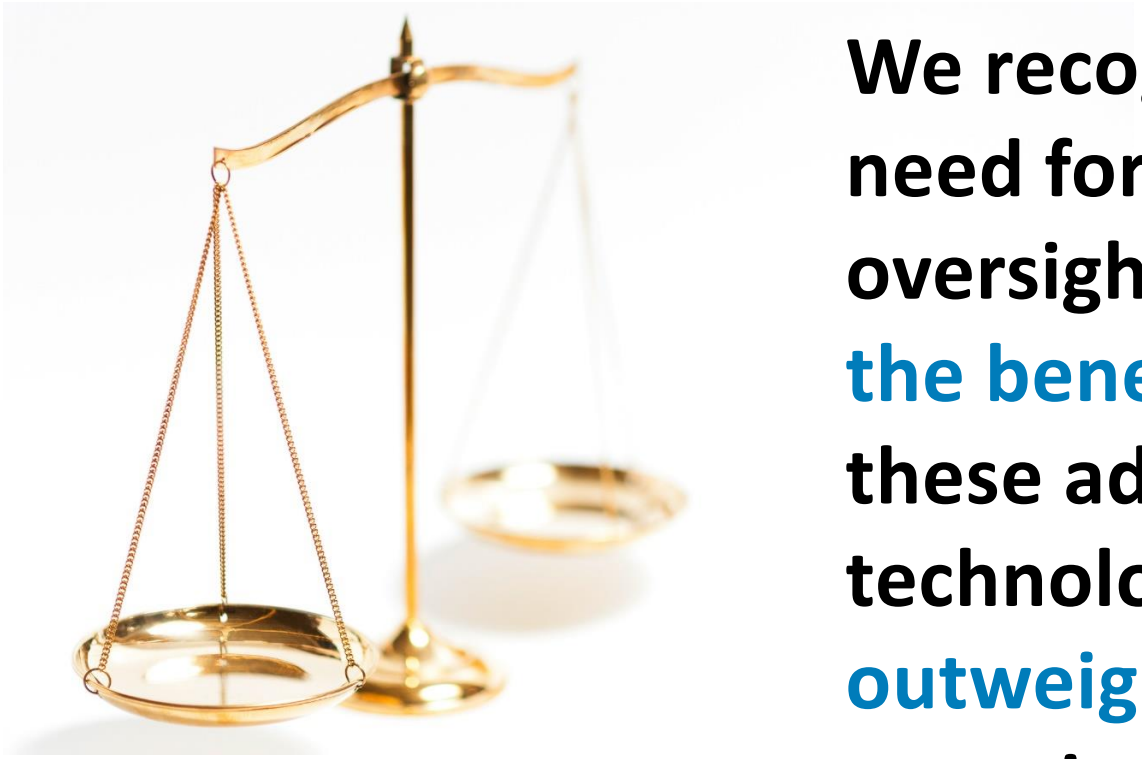
OPPORTUNITIES

- **Significant positive impact on health care**
  - Earlier disease detection
  - More accurate diagnosis
  - New insights into human physiology
  - Personalized diagnostics and therapeutics
- **Applications across all medical fields**
- **Ability to learn, adapt, and improve performance**

CHALLENGES

- **Fit-for-purpose data sets for development and testing, including diversity**
- **Identification and minimization of bias**
- **Opacity of some algorithms**
- **Providing oversight for an adaptive system**
- **Ensuring transparency to users**

Unique Considerations



We recognize the need for careful oversight to ensure the benefits of these advanced technologies outweigh the risks to patients.

- Usability
- Trust
- Equity
- Accountability

Proposing a Regulatory Framework

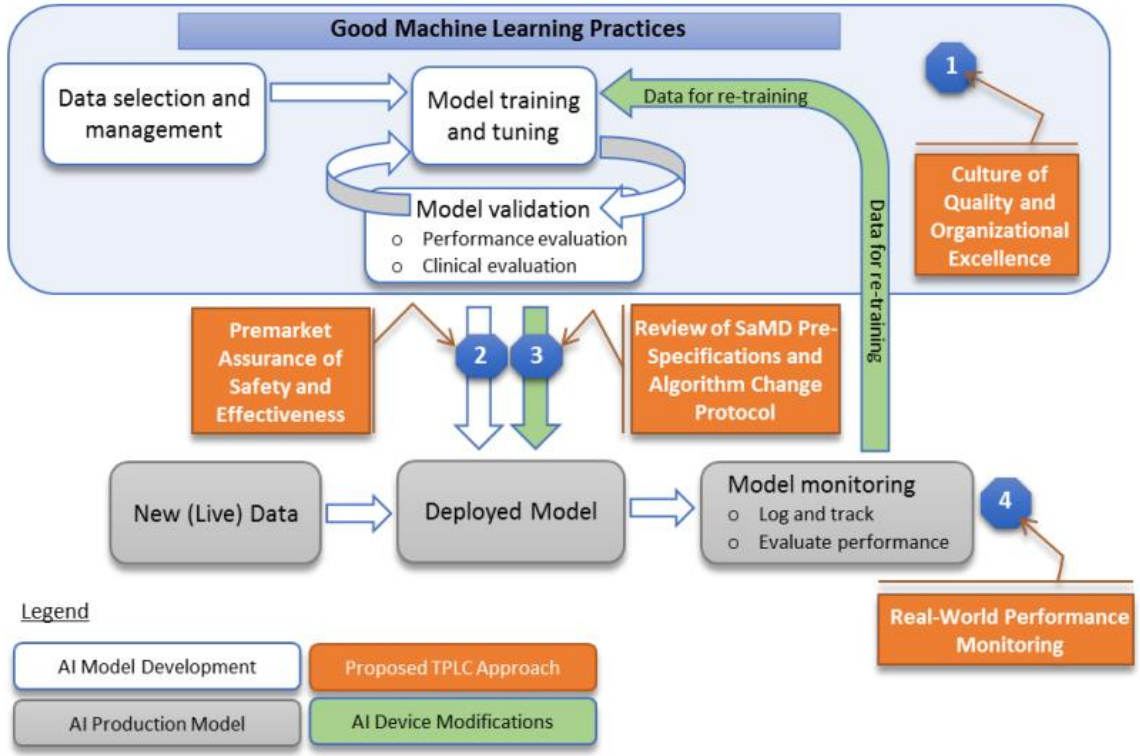


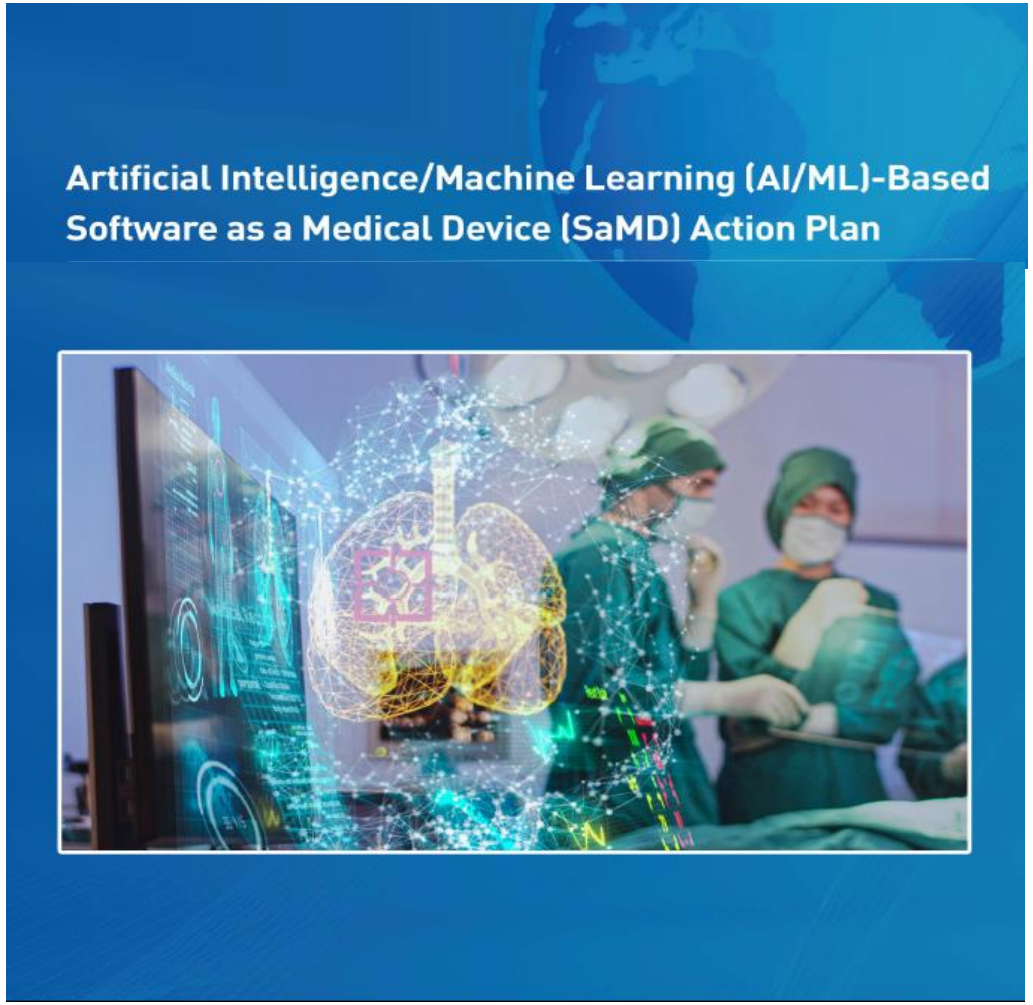
Figure 2: Overlay of FDA's TPLC approach on AI/ML workflow

Published in 2019

Discussion Paper and Request for Feedback

- Received stakeholder feedback through:
  - > 1,000 comments on public docket
  - > 30 publications in peer-reviewed journals
  - Pre-submission meetings on AI/ML devices
  - Patient Engagement Advisory Committee Meeting

Steps in Tailoring a Regulatory Framework



Published in 2021

Action Plan for AI/ML-Based SaMD

Outlines five next steps to advancing access:

1. Update the proposed AI/ML regulatory framework
2. Strengthen FDA's role in harmonizing GMLP
3. Foster a patient-centered approach
4. Support development of regulatory science methods
5. Advance real-world performance pilots

Continuing our Collaborative Approach to AI

Milestones

2019

- Published AI/ML-SaMD Discussion Paper
- First joined Collaborative Community related to AI/ML

2020

- Public Workshop on AI/ML in Radiological Imaging
- Patient Engagement Advisory Committee Meeting on Patient Trust in AI/ML Devices

2021

- Posted List of Currently Marketed AI/ML Devices
- Published AI/ML Medical Device Software Action Plan
- Public Workshop on Transparency of AI/ML Devices
- Published Good Machine Learning Practice Principles

2022

List Updated

- Contributed to IMDRF's Key Terms & Definitions: Machine Learning Enabled Medical Devices
- Published Clinical Decision Support (CDS) Final Guidance
- Recognized new Consensus Standard on AI/ML

2023

List Updated

- Published Predetermined Change Control Plan for AI/ML Devices Draft Guidance
- Announced formation of Digital Health Advisory Committee
- Published PCCP Guiding Principles

2024 (so far)

List Update

- Published AI & Medical Products paper on how FDA Centers are working together
- Developed AI and Medical Products page centralizing AI resources
- NPJ journal article on Transparency in AI/ML-enabled devices
- Published Transparency for Machine Learning-Enabled Medical Devices: Guiding Principles

Coming Soon

- Final guidance on PCCP for AI-enabled devices
- Draft guidance for Content and Lifecycle of AI-enabled devices
- First Digital Health Advisory Committee meeting
- IMDRF Good Machine Learning Principles

Future Plans (2024+)
AI/ML Medical Device Software Action Plan

- ❑ Develop AI quality assurance plan and infrastructure needs
- ❑ Strengthen FDA's role in harmonizing GMLP
- ❑ Foster a patient-centered approach
- ❑ Support development of regulatory science methods
- ❑ Advance real-world performance pilots

Predetermined Change Control Plans for AI/ML-enabled Devices

This draft guidance describes a least burdensome approach to support the iterative improvement of machine learning-enabled device software functions.

Contains Nonbinding Recommendations

Draft – Not for Implementation

Marketing Submission Recommendations for a Predetermined Change Control Plan for Artificial Intelligence/Machine Learning (AI/ML)-Enabled Device Software Functions

Draft Guidance for Industry and Food and Drug Administration Staff

DRAFT GUIDANCE

This draft guidance document is being distributed for comment purposes only.

Document issued on April 3, 2023.

You should submit comments and suggestions regarding this draft document within 90 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit electronic comments to https://www.regulations.gov. Submit written comments to the Dockets Management Staff, Food and Drug Administration, 5630 Fishers Lane, Room 1061, (HFA-305), Rockville, MD 20852. Identify all comments with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For questions about this document regarding CDRH-regulated devices, contact digitalhealth@fda.hhs.gov. For questions about this document regarding CBER-regulated devices, contact ocod@fda.hhs.gov. For questions about this document regarding CDER-regulated products, contact druginfo@fda.hhs.gov. For questions about this document regarding combination products, contact the Office of Combination Products at combination@fda.gov.

FDA U.S. FOOD & DRUG ADMINISTRATION

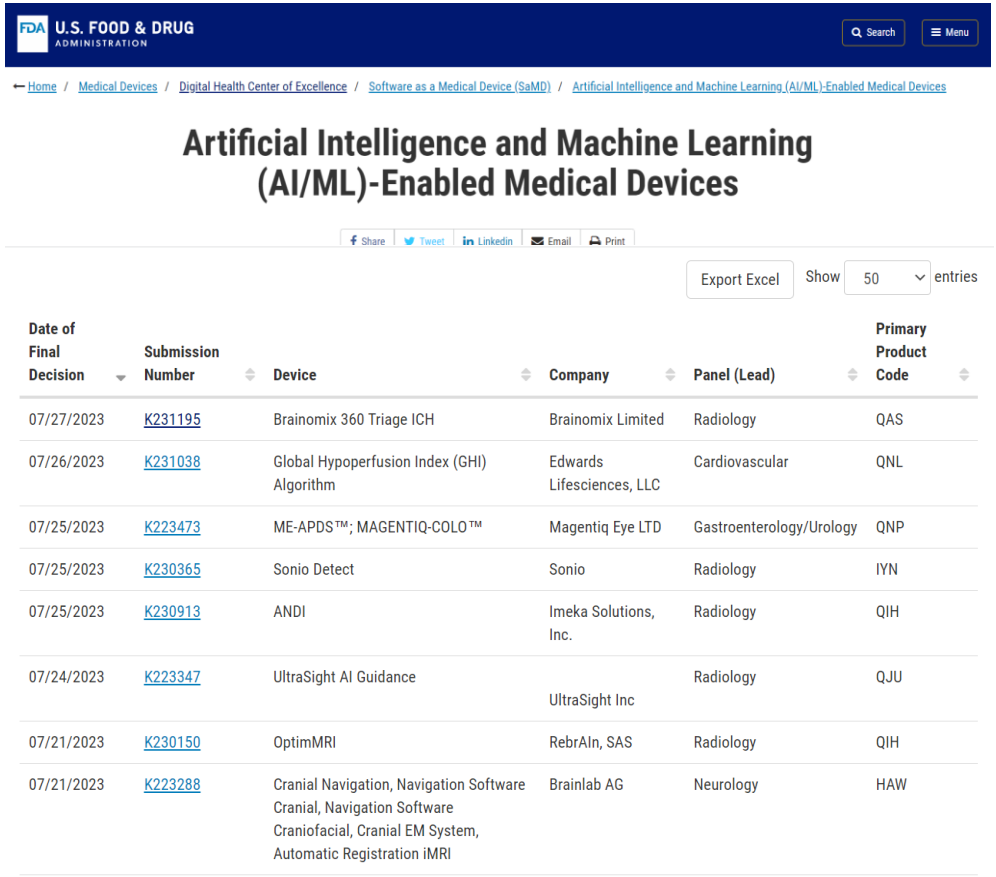
U.S. Department of Health and Human Services
Food and Drug Administration
Center for Devices and Radiological Health
Center for Biologics Evaluation and Research
Center for Drug Evaluation and Research
Office of Combination Products in the Office of the Commissioner

The FDA's proposed approach would:

- Put safe and effective advancements in the hands of health care providers and users faster.
- Ensure that important performance considerations with respect to race, ethnicity, disease severity, gender, age, and geographical consideration are addressed in AI/ML-enabled devices to better meet the needs of diverse populations.

Webinar: https://youtu.be/J26TfajAeSo
Guidance: https://www.fda.gov/medical-devices/digital-health-center-excellence/guidances-digital-health-content

Resources on AI/ML-Enabled Medical Devices



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Artificial Intelligence and Machine Learning (AI/ML)-Enabled Medical Devices

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Date of Final Decision	Submission Number	Device	Company	Panel (Lead)	Primary Product Code
07/27/2023	K231195	Brainomix 360 Triage ICH	Brainomix Limited	Radiology	QAS
07/26/2023	K231038	Global Hypoperfusion Index (GHI) Algorithm	Edwards Lifesciences, LLC	Cardiovascular	QNL
07/25/2023	K223473	ME-APDS™; MAGENTIQ-COLO™	Magentiq Eye LTD	Gastroenterology/Urology	QNP
07/25/2023	K230365	Sonio Detect	Sonio	Radiology	IYN
07/25/2023	K230913	ANDI	Imeka Solutions, Inc.	Radiology	QIH
07/24/2023	K223347	UltraSight AI Guidance	UltraSight Inc	Radiology	QJU
07/21/2023	K230150	OptimMRI	RebrAIn, SAS	Radiology	QIH
07/21/2023	K223288	Cranial Navigation, Navigation Software Cranial, Navigation Software Craniofacial, Cranial EM System, Automatic Registration iMRI	Brainlab AG	Neurology	HAW

Updated in August 2024

Currently Marketed AI/ML-Enabled Medical Devices

This list is meant to be:

1. A public resource on these devices and the FDA's work in this area
2. Show how AI/ML is being used across medical disciplines

A non-exhaustive list based on publicly available information

https://www.fda.gov/medical-devices/software-medical-device-samd/artificial-intelligence-and-machine-learning-aiml-enabled-medical-devices

Good Machine Learning Practice Principles

Published in 2021

U.S. FOOD & DRUG ADMINISTRATION | Health Canada Santé Canada | Medicines & Healthcare products Regulatory Agency

We envision these guiding principles may be used to:

- Adopt good practices that have been proven in other sectors;
- Tailor practices from other sectors so they are applicable to medical technology and the health care sector; and
- Create new practices specific for medical technology and the health care sector.

Good Machine Learning Practice for Medical Device Development: Guiding Principles	
Multi-Disciplinary Expertise are Leveraged Throughout the Total Product Life Cycle	**Good Software Engineering and Security Practices are Implemented**
Clinical Study Participants and Data Sets are Representative of the Intended Population	**Training Data Sets are Independent of Test Sets**
Selected Reference Datasets are Based Upon Best Available Methods	**Model Design is Tailored to the Available Data and Reflects the Intended Use of the Device**
Focus is Placed on the Performance of the Human-AI Team	**Testing Demonstrates Device Performance during Clinically Relevant Conditions**
Users are Provided Clear, Essential Information	**Deployed Models are Monitored for Performance and Re-training Risks are Managed**

https://www.fda.gov/medical-devices/software-medical-device-samd/good-machine-learning-practice-medical-device-development-guiding-principles

IMDRF

International Medical Device Regulators Forum

Artificial Intelligence Working Group

Working Group Goal

Achieve a harmonized approach to the management of Artificial Intelligence (AI) medical devices.

Benefit

Traditional regulatory approaches are inappropriate to efficiently manage machine learning enabled medical devices and many jurisdictions have developed their own approaches to the regulation of machine learning enabled medical devices. This work is the first step that can ensure a more globally harmonized approach for handling machine learning enabled devices.

Current Work Item

Revise and update the 2021 Good Machine Guiding Principles (GMLP) building on existing work and incorporating updates based on recent advances in AI including generative and AI/ large language models (LLMs). Expected publication end of 2024.

New Work Item Proposal

To provide an internationally harmonized AI lifecycle technical framework to help promote responsible innovation, health equity, and patient-centricity by facilitating the secure, safe, ethical, and effective development, deployment, maintenance, and use of AI-enabled medical devices.

IMDRF

International Medical Device Regulators Forum

Software as a Medical Device (SaMD) Working Group

Working Group Goal

To support innovation and timely access to safe and effective SaMD globally by identifying commonalities, establishing a common vocabulary, and developing approaches for appropriate regulatory controls that promote regulatory convergence.

Current Work Item

IMDRF N81, *Medical Device Software: Considerations for Device and Risk Characterization* completed its public consultation in May 2024 and is addressing the feedback received. Expected publication end of 2024.

This new document promotes and informs clear and accurate characterizations of medical device software (including intended use/intended purpose statements and device descriptions). It also introduces a general strategy for characterizing software-specific risks that leverages the key features of a comprehensive medical device software characterization.

New Work Item Proposal

This document is to provide internationally harmonized high-level guidelines on what should be included in a Predetermined Change Control Plans (PCCP) for software-related changes, including changes related to artificial intelligence considerations and identify best practices for developing and documenting a PCCP. The document will develop a broad but harmonized framework for PCCPs allowing each jurisdiction to apply the concepts within the scope of regulations applicable to their jurisdiction.

For more information....

IMDRF Software as a Medical Device (SaMD) Working Group

- Sonja Fulmer (US FDA) Sonja.Fulmer@fda.hhs.gov
- Marc Lamoureux (Health Canada) Marc.Lamoureux@hc-sc.gc.ca

IMDRF Artificial Intelligence (AI) Working Group

- Matt Diamond (US FDA) Matthew.Diamond@fda.hhs.gov
- Russell Pearson (UK MHRA) Russell.Pearson2@mhra.gov.uk

We provide digital health stakeholders ongoing clarity through guidance

15 Digital Health Guidance Documents Published Since FY2018

GUIDANCE DOCUMENT

Content of Premarket Submissions for Device Software Functions

Draft Guidance for Industry and Food and Drug Administration Staff

GUIDANCE DOCUMENT

Clinical Decision Support Software

GUIDANCE DOCUMENT

Cybersecurity in Medical Devices: Quality System Considerations and Content of Premarket Submissions

GUIDANCE DOCUMENT

Changes to Existing Medical Software Policies Resulting from Section 3060 of the 21st Century Cures Act

GUIDANCE DOCUMENT

Medical Device Accessories - Describing Accessories and Classification Pathways

DRAFT

GUIDANCE DOCUMENT

Marketing Submission Recommendations for a Predetermined Change Control Plan for Artificial Intelligence/Machine Learning (AI/ML)-Enabled Device Software Functions

GUIDANCE DOCUMENT

Policy for Device Software Functions and Mobile Medical Applications

GUIDANCE DOCUMENT

Digital Health Technologies for Remote Data Acquisition in Clinical Investigations

Draft Guidance for Industry, Investigators, and Other Stakeholders

GUIDANCE DOCUMENT

General Wellness: Policy for Low Risk Devices

GUIDANCE DOCUMENT

Software as a Medical Device (SAMD): Clinical Evaluation

GUIDANCE DOCUMENT

Cybersecurity in Medical Devices: Refuse to Accept Policy for Cyber Devices and Related Systems Under Section 524B of the FD&C Act

GUIDANCE DOCUMENT

Medical Device Data Systems, Medical Image Storage Devices, and Medical Image Communications Devices

GUIDANCE DOCUMENT

Multiple Function Device Products: Policy and Considerations

GUIDANCE DOCUMENT

Off-The-Shelf Software Use in Medical Devices

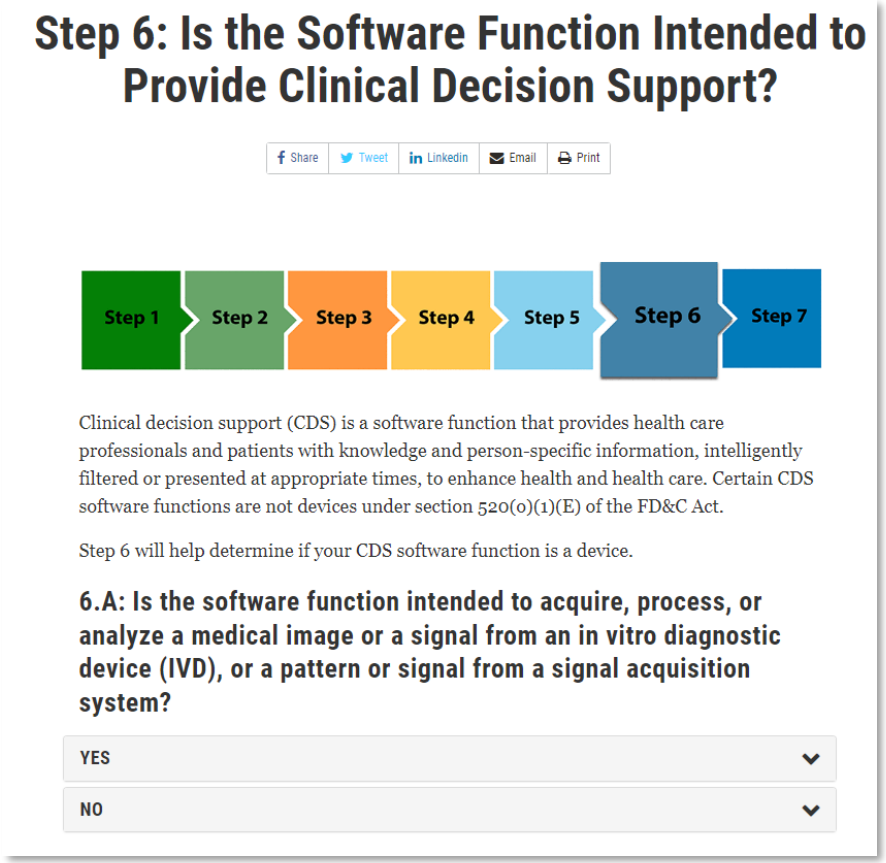
GUIDANCE DOCUMENT

Deciding When to Submit a 510(k) for a Software Change to an Existing Device

Digital Health Policy Navigator

https://www.fda.gov/medical-devices/digital-health-center-excellence/digital-health-policy-navigator

- A public facing tool to help in determining whether a product's software functions are potentially the focus of the FDA's oversight
- The Digital Health Policy Navigator provides considerations for whether a software function is potentially subject to or the focus of FDA's regulatory oversight as a device. The Digital Health Policy Navigator does not address:
  - Considerations on how to design, develop, and test software functions; or
  - Considerations relating to the regulation of software used with other medical products (e.g., drugs, biologics), or software intended for other purposes (e.g., electronic consent forms).
- The Navigator includes seven steps, each with a set of questions intended help guide you through the most relevant FDA medical device regulatory considerations and guidance documents.



Further Questions or Feedback

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Digital Health Center of Excellence (DHCoE)

Center for Devices and Radiological Health, U.S. Food and Drug Administration

Thank You/Questions?