Google Health

Regulating AI/ML-SaMD in the US

Outlook towards generative AI based solutions

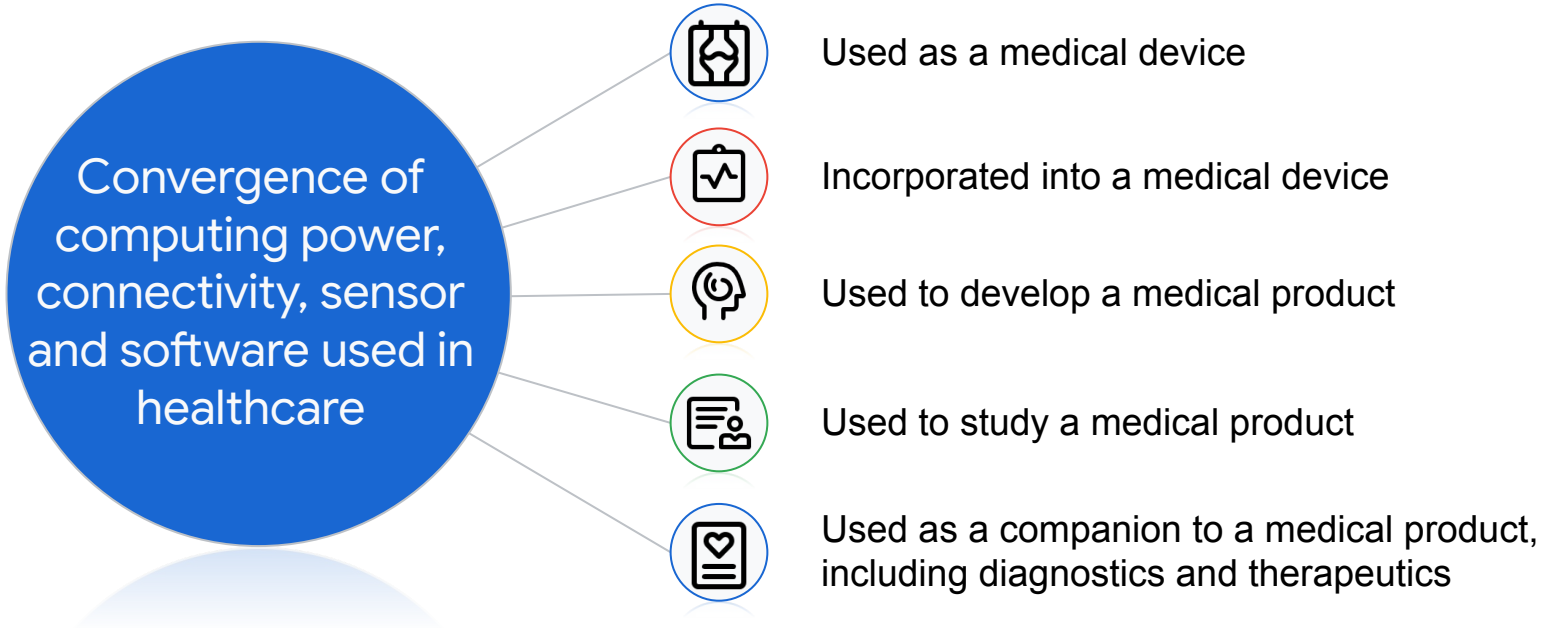
Presentation Outline

1. US FDA journey and intent
    a. FDA: Enabling Innovative Software technologies
2. AI/ML-enabled Medical Device
    a. Approach - proposal - changes and monitoring
    b. Predetermined Change Control Plan (PCCP)
    c. Real world monitoring
3. Outlook on Regulating Generative AI
    a. Understanding Generative and Predictive AI
    b. Limitations of PCCP and real world monitoring
    c. Considering a different way to regulate

US FDA journey and intent

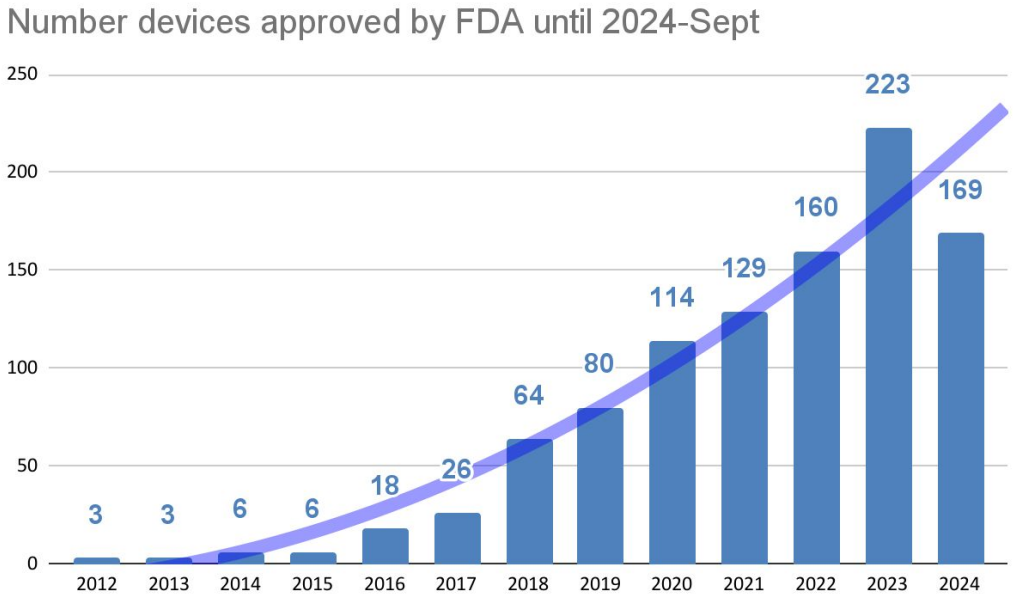
Digital Health Technology

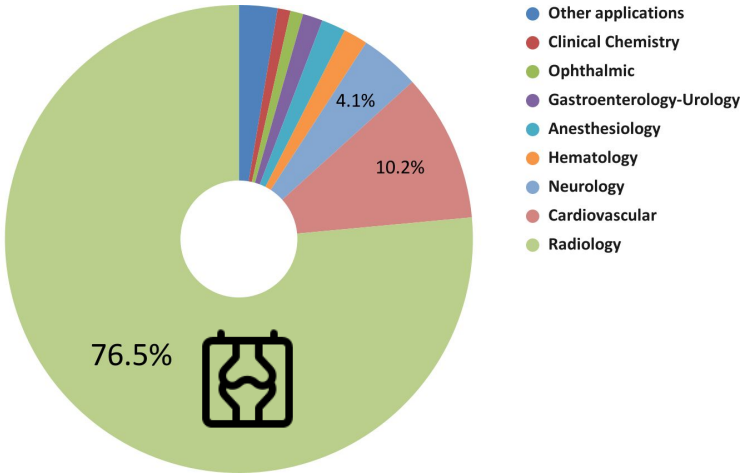
Healthy living → Prevention → Diagnosis → Recovery → Home Care → Management



FDA-Approved AI/ML-SaMD in the US

More than 1000 AI/ML-enabled medical device has been placed on the US market until 2024-September, majority (76.5 %) is based on radiology application.



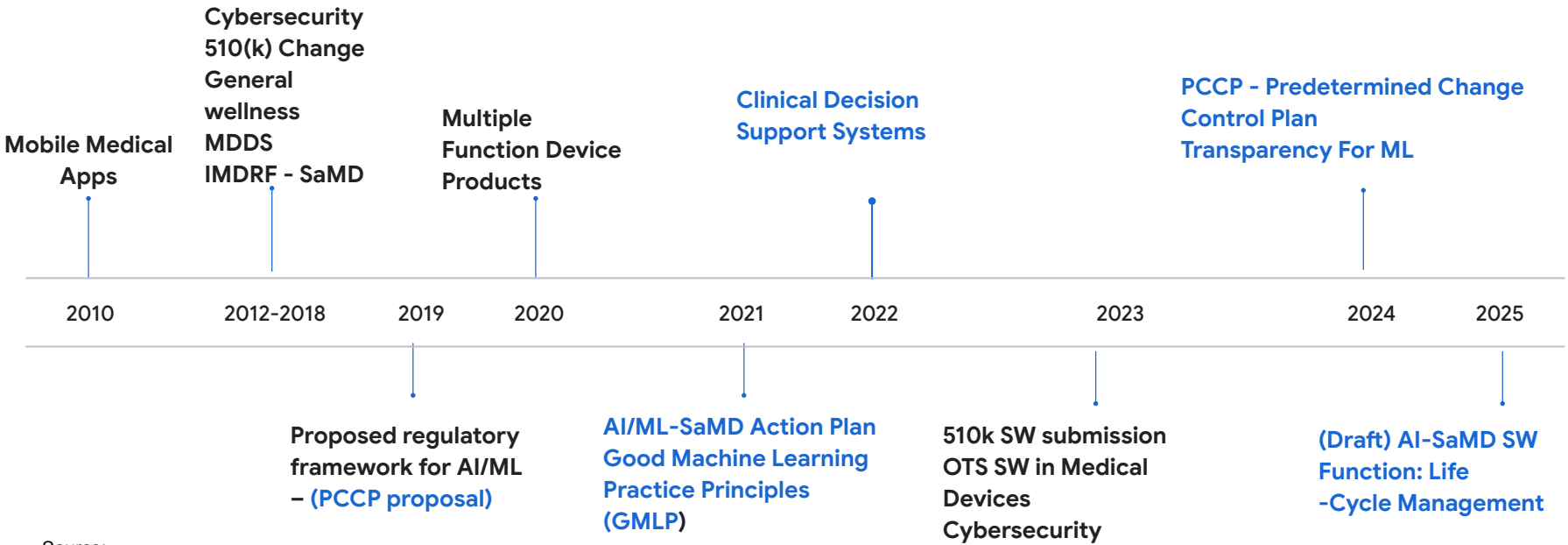


Source; https://www.fda.gov/medical-devices/software-medical-device-samd/artificial-intelligence-and-machine-learning-aiml-enabled-medical-devices

FDA: Enabling Innovative Software technologies

Evolution of FDA's approach following Software and AI technology

FDA pro-actively published new documents and revised existing ones as technology advanced

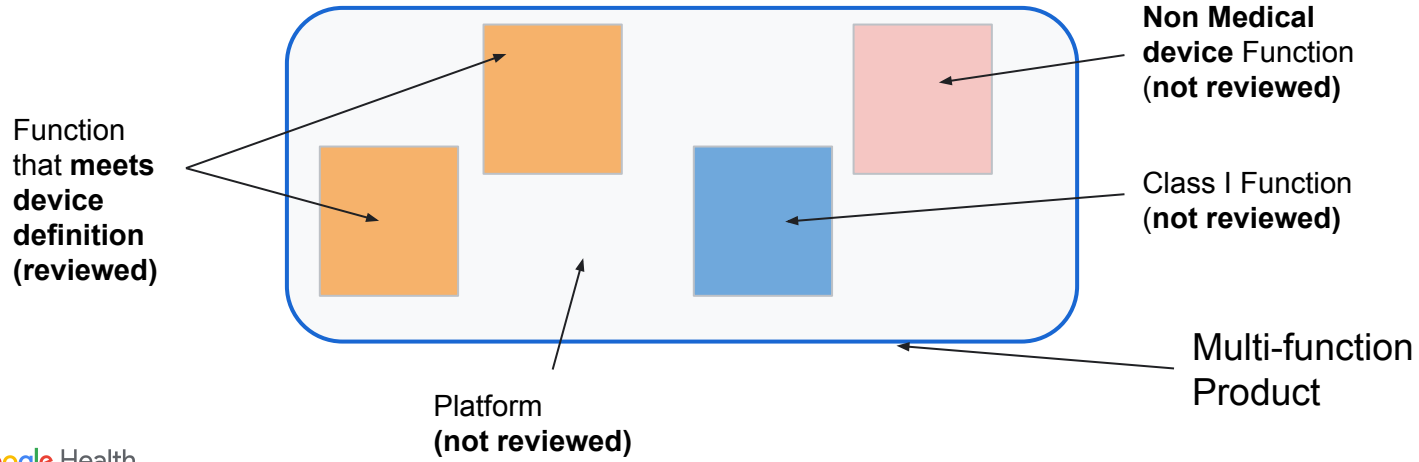


Source:
AI & ML in SaMD: https://www.fda.gov/medical-devices/software-medical-device-samd/artificial-intelligence-and-machine-learning-software-medical-device
Guidances with Digital Health Content: https://www.fda.gov/medical-devices/digital-health-center-excellence/guidances-digital-health-content

2012 FDA: Introduces “Function” based regulation

Adopted in 2016 law –
In multiple function guidance “function” is described as – is a distinct purpose of ,

- which could be the intended use, or
- a subset of the intended use of the product”



2019 – Proposed regulatory approach for AI/ML

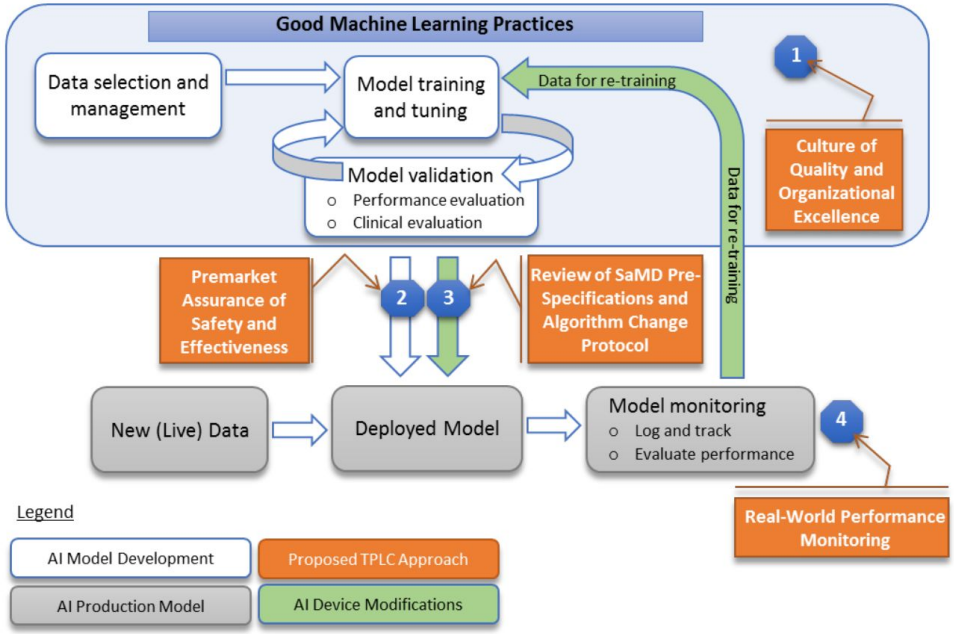


Figure 2: Overlay of FDA's TPLC approach on AI/ML workflow

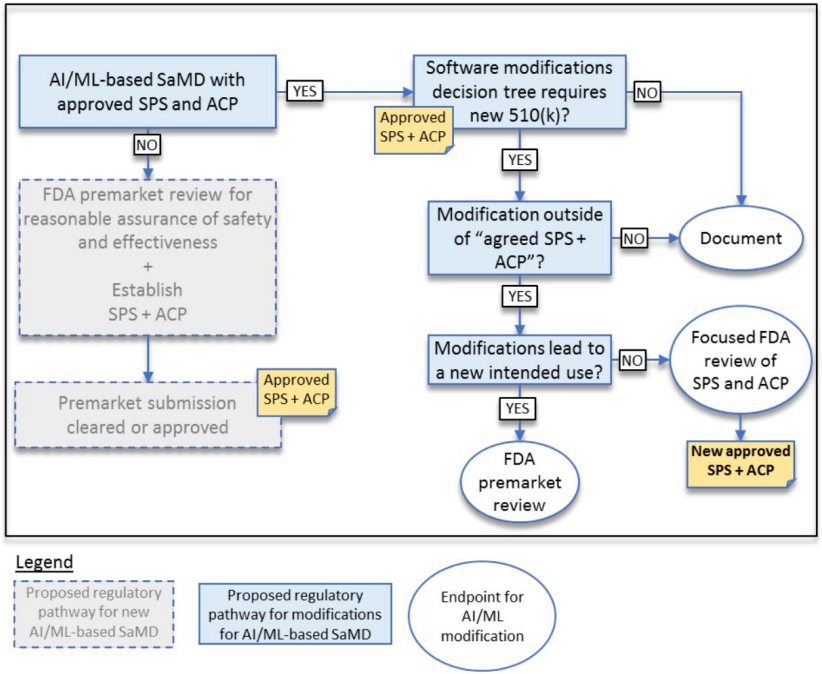
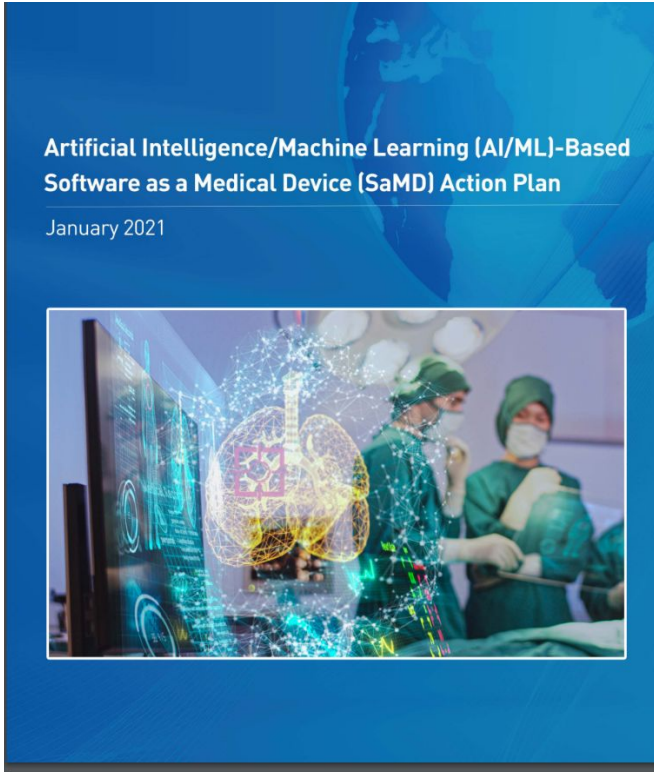


Figure 5: Approach to modifications to previously approved SaMD with SPS and ACP. This flowchart should only be considered in conjunction with the accompanying text in this white paper.

FDA's AI/ML-SaMD Action Plan (2021 January)

"The FDA's traditional paradigm of medical device regulation was not designed for adaptive artificial intelligence and machine learning technologies."

- **GMLP** (Good Machine Learning Practice): collaborative communities and consensus standards development
- **PCCP**: Predetermined change control plan allowing post-market changes
- **Transparency**: Patient-centered approaches with public discussions to build patient trust and awareness in AI/ML technologies
- **Performance and Trustworthiness:** Establishing communities to AL/ML algorithm performance and matrices
- **RWE**: Promote Real-World Evidence generation programs in collaboration with stakeholders



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Source: https://www.fda.gov/media/145022/download

Good Machine Learning Practice for Medical Device Development: Guiding Principles (2021 October)

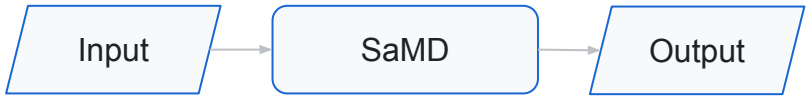
The U.S. Food and Drug Administration (FDA), Health Canada, and the United Kingdom's Medicines and Healthcare products Regulatory Agency (MHRA) have jointly identified 10 guiding principles that can inform the development of Good Machine Learning Practice (GMLP).

1. **Multi-Disciplinary Expertise** Is Leveraged Throughout the Total Product Life Cycle
2. Good Software Engineering and **Security Practices** Are Implemented
3. Clinical Study Participants and **Data Sets Are Representative of the Intended Patient Population**
4. **Training Data Sets Are Independent of Test Sets**
5. Selected Reference Datasets Are Based Upon **Best Available Methods**
6. **Model Design** Is Tailored to the Available Data and **Reflects the Intended Use** of the Device
7. Focus Is Placed on the **Performance of the Human-AI Team**
8. Testing Demonstrates Device **Performance during Clinically Relevant Conditions**
9. **Users Are Provided Clear, Essential Information**
10. Deployed Models Are Monitored for Performance and Re-training **Risks are Managed**

AI/ML enabled - Software as Medical Device

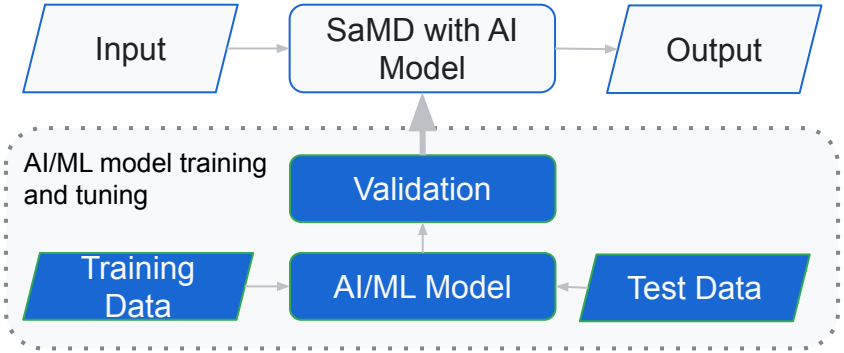
“Conventional” SaMD vs AI/ML-enabled SaMD

“Conventional” SaMD



- Deterministic algorithm
- Exact input and output functions
- No post-deployment adaptation

AI/ML-enabled SaMD



- Probabilistic or stochastic algorithms
- Quality of output significantly depends on training/testing/validation data sets and underlying model architecture
- Post-deployment adaptation are possible depending on the model and the software

“Locked” vs “Adaptive System”

Manufacturer / Provider

End User

LOCKED

New Data → **Re-trained AI/ML Model** → Deploy model → **SaMD in use** [**Fine Tuned AI/ML Model**]

New Data → **Fine Tuned AI/ML Model**

ADAPTIVE

Not aware of any used as SaMD

Initial AI/ML Model → Deploy model → **SaMD in use** [**Fine Tuned AI/ML Model**]

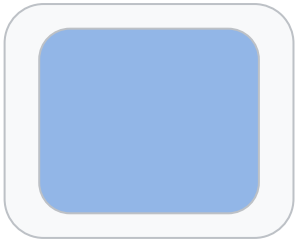
New Data → **Fine Tuned AI/ML Model**

These systems aim to continuously learn based on new data at runtime to adapt more quickly to changes in real-world circumstances.

Predetermined Change Control Plan (PCCP) - AI/ML

Locked

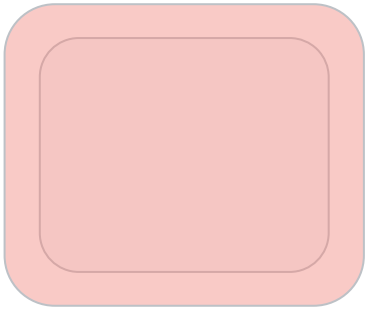
No changes after the product is deployed



Allowed - PCCP

Within Predetermined Change Boundaries:

- New source to obtain same input data
- Addition of new user-interface



Not allowed

Change Outside of the predefined boundaries:

- Change to intended purpose
- New clinically relevant data input type is used
- Significant change SW architecture, alarm system etc.
- Impairment of safety and effectiveness

PCCP Example

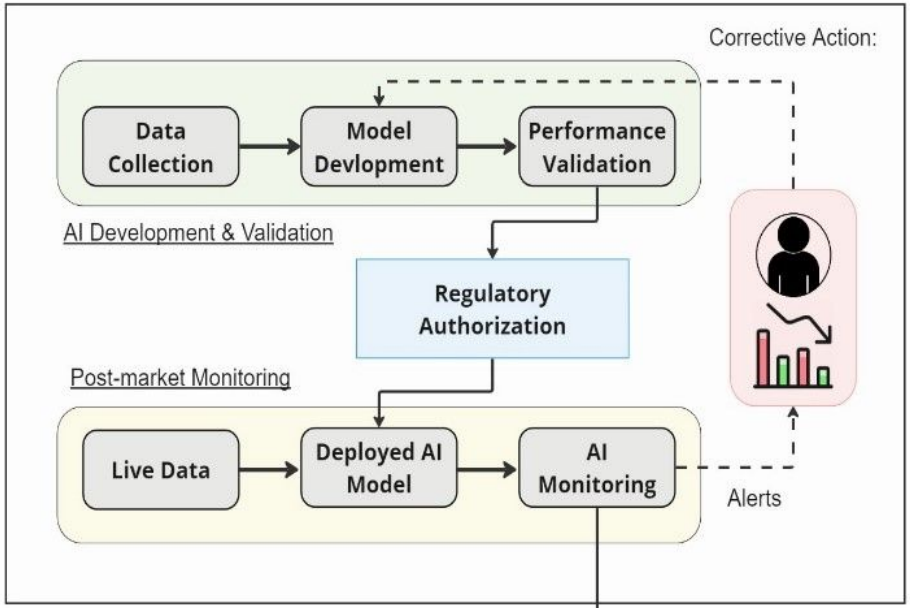
Background: The device is an AI-DSF that analyzes images of skin lesions by identifying and characterizing its features (e.g., color, quantification of area change over time) to aid in diagnosis. It was validated with a specific camera and is intended to be used by a primary healthcare provider. The AI-enabled medical device was authorized with a PCCP.

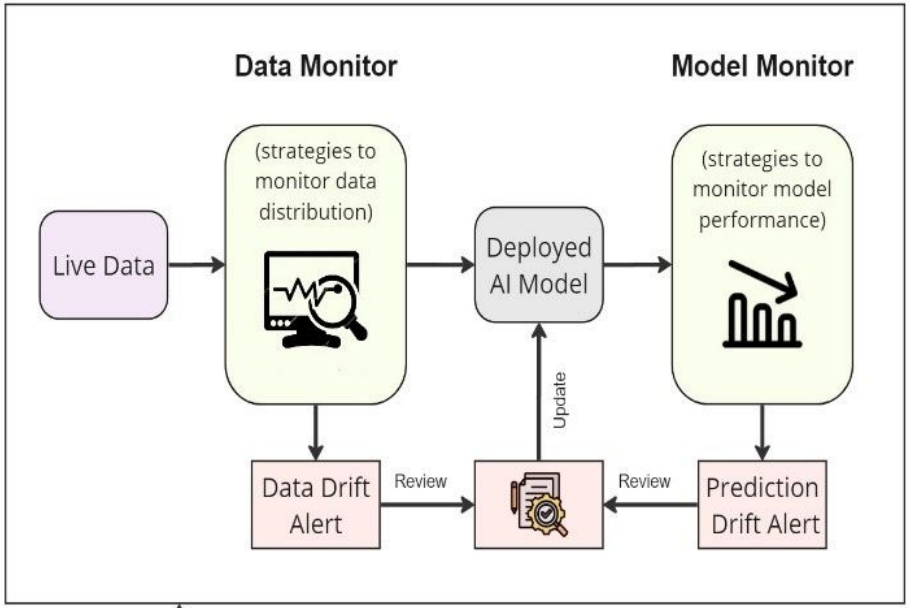
Brief Overview of Pre-Specified Modification: The manufacturer would like to extend the AI-DSF for use on additional general-purpose computing platforms, including smartphones and tablets. The general-purpose **computing platform must include a two-dimensional camera that meets the minimum specifications defined in the PCCP**. The updated device must achieve a **minimum performance defined in the Modification Protocol using a specified methodology**.

Post-Authorization Modification Scenarios: Modification Scenario 1: **Modification in input, as specified in the PCCP and implemented in accordance with the PCCP**

Source: **Marketing Submission Recommendations for a Predetermined Change Control Plan for Artificial Intelligence-Enabled Device Software Functions,** https://www.fda.gov/media/166704/download

Real world monitoring





Source:https://www.fda.gov/medical-devices/medical-device-regulatory-science-research-programs-conducted-osel/methods-and-tools-effective-postmarket-monitoring-artificial-intelligence-ai-enabled-medical-devices

Outlook on Regulating Generative AI

“Predictive AI” vs “Generative AI”

Predictive AI

- Execute a specific task efficiently
- Defined output based on predefined programmed task
- Clear intended purpose, patient population, or clinical conditions

E.g Radiology devices e.g. AI/ML-based image recognition.

Generative AI

- Produce new content based on existing data
- “Novel outputs” that may not be directly predicted
- Intended purpose can be broad and less specific than those for “narrow AI” applications.

E.g. LLM based applications trained on large set-of clinical and health data

Generative AI is making a significant impact in healthcare

AI products are being developed to synthesize complex medical information

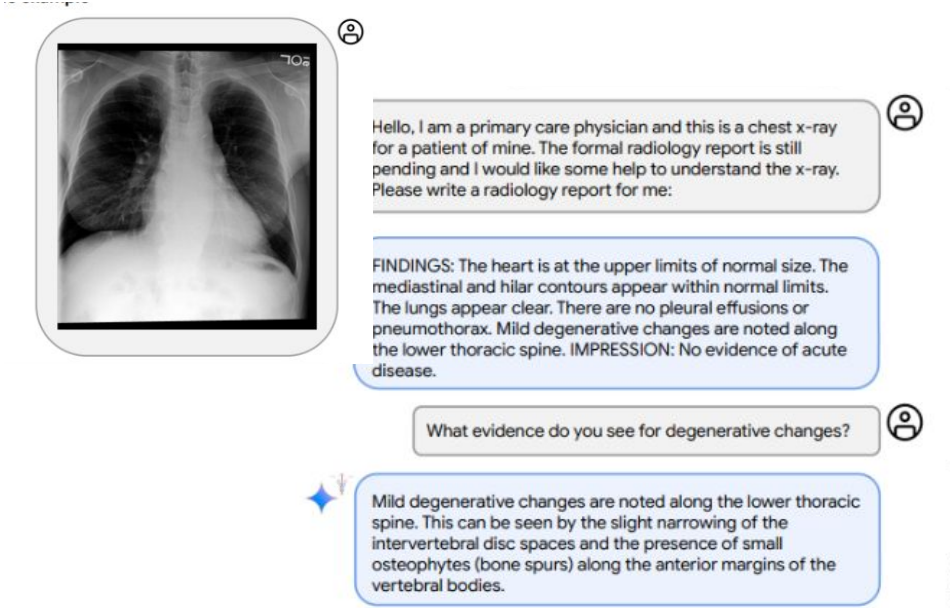
Research organizations are interested in leveraging AI to support drug development

AI-powered predictive models and analytics can help detect health trends and outcomes

AI software is being created to support provider education and improve patient care

Generative Artificial Intelligence (Generative AI)

"The class of AI models that emulate the structure and characteristics of input data in order to generate derived synthetic content. This can include images, videos, audio, text, and other digital content." (Source: E.O. 14110)
This is usually done by approximating the statistical distribution of the input data. For example, in healthcare, generative AI can be used to generate annotations on synthetic medical data (e.g., image features, text labels) to help expand datasets for training algorithms. "

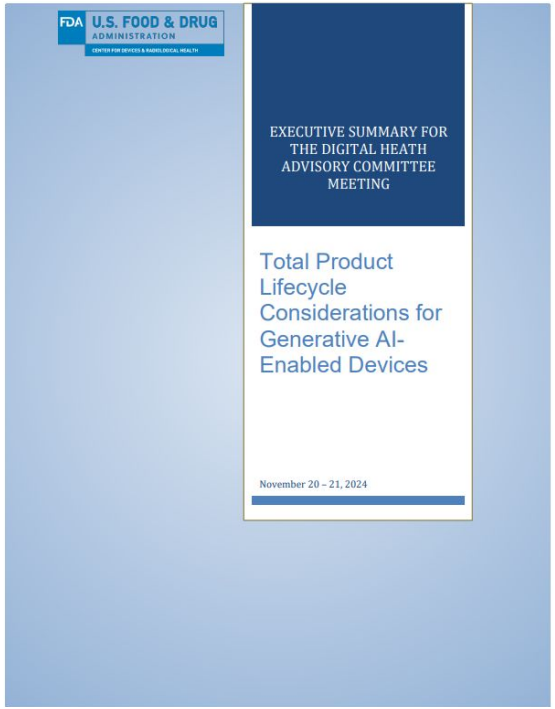


Source:https://www.fda.gov/science-research/artificial-intelligence-and-medical-products/fda-digital-health-and-artificial-intelligence-glossary-educational-resource#:~:text=Artificial%20Intelligence%20(AI)&text=Artificial%20intelligence%20systems%20use%20machine,options%20for%20information%20or%20action.

Source: Capabilities of Gemini Models in Medicine, https://arxiv.org/pdf/2404.18416 (last visited 2025-01-25)

FDA faces challenges with approval of Generative AI-enabled Devices

- **Specific risks and complexities** regarding Generative AI-enabled devices
- **Application of risk-based approach** to classification and determining regulatory requirements
- Determining the types of valid scientific evidence for the **evaluation of the safety and effectiveness**.
- Determining **valid clinical associations**



Source: Total Product Lifecycle Considerations for Generative AI-Enabled Deviceshttps://www.fda.gov/media/182871/download

Limitations of PCCP and real world monitoring

1. **Scope of changes**: PCCPs are generally not suitable for introducing new risks to the device, changes to intended purpose including changes to for example additional new data inputs / types.
2. **Number of modifications**: Only a limited number of modifications via PCCP is recommended
3. **Continuous learning AI systems**: Currently FDA has limited capability to assess safety and effectiveness of such devices
4. **Increased submission complexity**: PCCP can increase complexity and prolong submission reviews

3 Epochs of AI + AGI

JAMA. 2024;331(3):242-244. doi:10.1001/jama.2023.25057 - Howell, Corrado, DeSalvo

The Rule-Based Beginnings

1.0

AI 1.0 includes symbolic AI, which attempts to encode human knowledge into computational rules, and introduces probabilistic models. This era laid the groundwork for AI by emphasizing logic and structured decision-making.

The Deep Learning Revolution

2.0

The era of AI 2.0 began with the advent of deep learning. Here, models learn from examples labeled with ground truths, leading to significant advancements in daily life and healthcare. Deep learning models are task-specific, focusing on classification and prediction.

The Age of Foundation Models and Generative AI

3.0

AI 3.0 introduces us to foundation models and generative AI, bringing transformative capabilities and new risks like hallucinations. These models can do many different kinds of tasks without being retrained on new datasets. For example, these models can perform various tasks with simple text instructions, adapting their output based on the context. For example, instructing a model to write a note for a specialist consultant versus a patient's mother yields significantly different results.

Artificial General Intelligence (AGI)

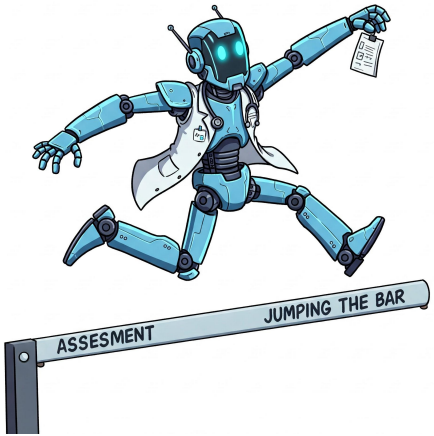
4.0

.Artificial general intelligence (AGI) refers to the hypothetical intelligence of a machine that possesses the ability to understand or learn any intellectual task that a human being can. Advancements in these areas are continuously shaping our understanding and the development of AGI. Currently, AGI remains largely a concept and a goal that researchers and engineers are working towards.

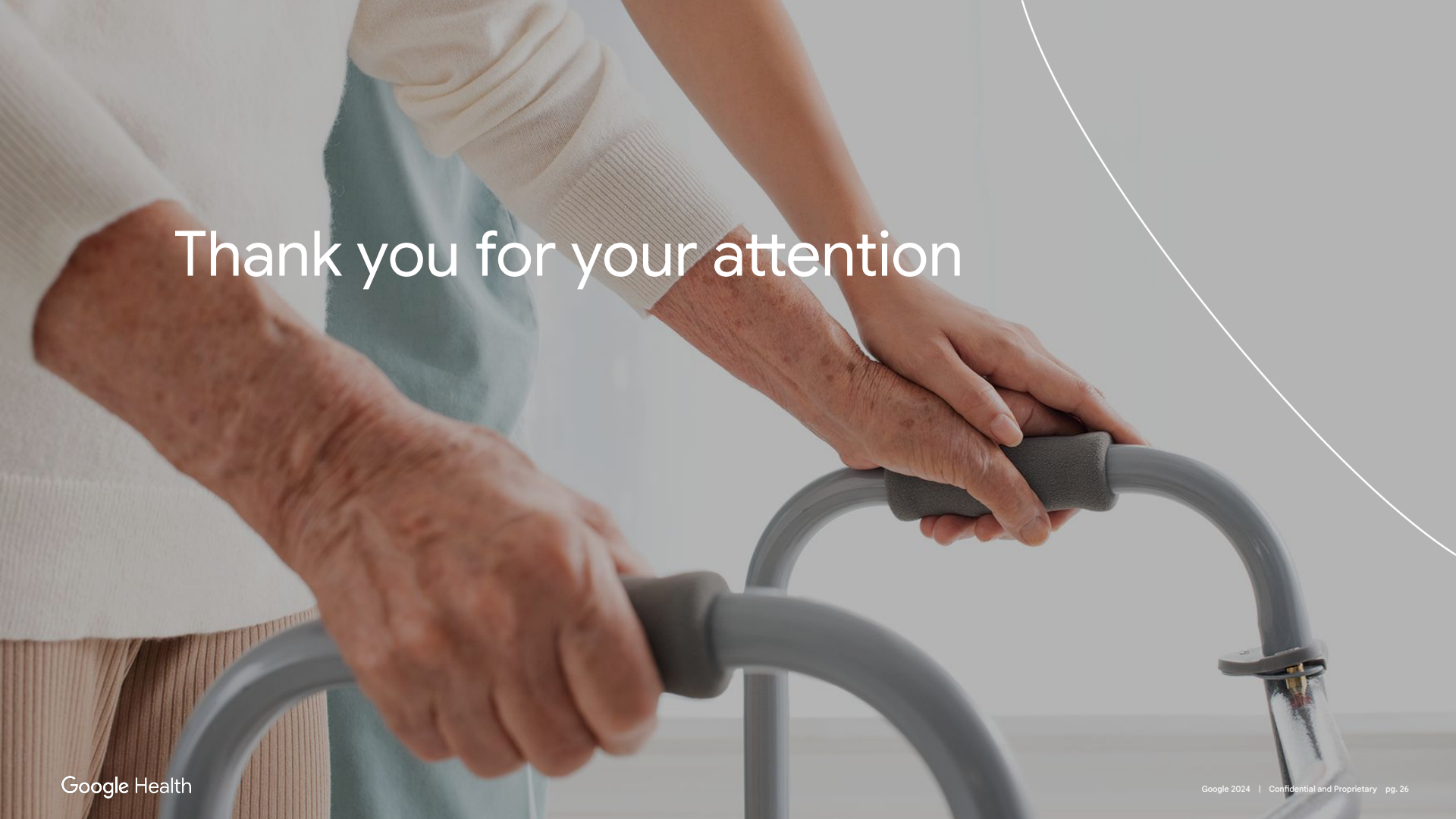
Considering a different way to ~~regulate~~ systematically oversee GenAI

"Treat these GAI-based clinical applications not as devices but as a **new type of clinical intelligence**: that is, to **regulate them less like devices and more like clinicians.**"

- Specialized Training in Clinical Practice
- Passing Relevant Clinical Exams
- Supervised Use with Clinician Oversight
- Regular Updates, Retesting, and Reevaluation
- Reporting on Quality of Care to Authorities
- Public Availability of Evaluation Results



Source:The Regulation of Clinical Artificial Intelligence - https://ai.nejm.org/doi/10.1056/AIpc2400545
The Regulation of Clinical Artificial Intelligence https://hbr.org/2024/09/how-to-regulate-generative-ai-in-healthcare, (Last visited 2025-01-25)


Thank you for your attention