

REGULATORY INTELLIGENCE

AI-Driven Medical Device Registration in the United States

FDA Pathways, AI/ML Framework, GMLP Standards & Submission Requirements

Jurisdiction	Authority	Device Type	Report Date	Version
United States	FDA / CDRH	AI/ML-Based SaMD	July 2026	V.1

EXECUTIVE SUMMARY

The FDA regulates AI-driven medical devices primarily under the **Software as a Medical Device (SaMD)** framework. With over 500+ AI/ML-enabled devices authorized as of Q1 2024, the regulatory landscape has matured significantly, anchored by the 2021 AI/ML Action Plan, Good Machine Learning Practice (GMLP) guiding principles, and the 2023 Predetermined Change Control Plan (PCCP) guidance.

This report covers the full registration lifecycle — from device classification and premarket pathways to post-market surveillance requirements and recent regulatory developments through early 2025.

500+

AI/ML Devices Authorized (Q1 2024)

~75%

Radiology / Imaging Devices

~85%

Cleared via 510(k) Pathway

+30%

YoY Growth in Authorizations

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2. Device Classification System

FDA uses a three-class risk-based system. Most AI/ML medical devices fall into **Class II**, requiring 510(k) clearance or De Novo authorization.

Class	Risk Level	Regulatory Control	Common Pathway	Examples (AI)
Class I	Low	General controls only	Exempt or 510(k)	Fitness/wellness apps, low-risk monitoring
Class II	Moderate	General + Special controls	510(k) or De Novo	AI radiology, dermatology, ECG analysis
Class III	High	Premarket Approval (PMA)	PMA	AI-driven cardiac implant systems

SaMD Applicability: Per IMDRF and FDA, Software as a Medical Device (SaMD) is "software intended to be used for one or more medical purposes that perform these purposes without being part of a hardware medical device." AI/ML-based SaMD is subject to all SaMD regulations.

SaMD Risk Evaluation Framework

FDA evaluates AI SaMD based on three dimensions:

Dimension	Options	Impact on Review
Intended use	Treat/diagnose/monitor/prevent	Higher use = more scrutiny
Healthcare situation	Critical / Serious / Non-serious	Critical = highest risk tier
State of condition	Critical / Stable / Non-serious	Informs clinical risk level

3. Premarket Pathways for AI Devices

510(k) — Premarket Notification MOST COMMON ~85% of AI device clearances

Requires demonstration of **substantial equivalence** to a legally marketed predicate device. FDA reviews within 90 days (standard) or 30 days (abbreviated/special). AI-specific: algorithm training data, validation datasets, and performance metrics must be fully documented. Most Class II AI diagnostics use this pathway.

De Novo — Novel Low-to-Moderate Risk GROWING ~10% of AI authorizations | ~150 day avg timeline

Used when **no predicate device exists** but the device is low-to-moderate risk. FDA classifies the device and sets special controls — often including AI-specific performance standards. Increasingly used for first-of-kind AI imaging and diagnostic tools. Creates a new regulatory classification that others can use as predicate.

PMA — Premarket Approval HIGH RISK Class III only | ~5% of AI devices | 180 day review

Required for **Class III AI devices** — high-risk, life-sustaining, or implantable. Most rigorous pathway: requires valid scientific evidence of safety and effectiveness from clinical studies. Rarely used for AI-only devices; more common for AI components in implantable/life-support systems.

Breakthrough Device Designation PRIORITY REVIEW Optional expedited pathway

Available for AI devices providing **more effective treatment/diagnosis of life-threatening or irreversibly debilitating conditions**. Grants priority review, increased FDA interaction during development, rolling submission (review sections as submitted). FDA has granted Breakthrough designation to dozens of AI diagnostic tools in radiology, pathology, and cardiology.

Locked vs. Adaptive Algorithms

Type	Definition	Regulatory Treatment
Locked Algorithm	Does not change after deployment; fixed parameters	Standard device review via applicable pathway
Adaptive Algorithm	Continues to learn/change in production environment	Predetermined Change Control Plan (PCCP) required

4. AI/ML-Specific Regulatory Framework

4.1 AI/ML Action Plan (January 2021) — 5 Pillars

01

Tailored Regulatory Framework

Addressing locked vs. adaptive algorithms; framework for continuously learning AI systems without requiring new submissions for every update

02

Good Machine Learning Practice (GMLP)

Standards for responsible AI development — data quality, training methodology, validation, bias detection, and lifecycle management

03

Patient-Centered Approach

Transparency requirements, algorithmic bias awareness, patient safety as design priority, meaningful patient/caregiver input

04

Regulatory Science Methods

Developing methods to evaluate AI performance, test for bias, and assess real-world algorithm behavior in diverse populations

05

Real-World Performance (RWP) Monitoring

Post-market surveillance specific to AI devices — tracking distribution shift, dataset drift, demographic performance changes, and algorithm degradation over time

4.2 Predetermined Change Control Plan (PCCP)

Introduced in FDA Guidance (2023): Allows manufacturers to pre-specify how an AI algorithm can change **without requiring a new 510(k) submission**. Critical for adaptive/continuously learning AI systems. The PCCP must describe: (1) anticipated modifications, (2) methodology for implementing changes, and (3) performance evaluation methods for each modification type.

5. Key Guidance Documents

Document	Year	Status	Key Focus
Proposed Regulatory Framework for AI/ML SaMD	2019	DISCUSSION PAPER	Locked vs. adaptive concepts; framework foundations
AI/ML Action Plan	Jan 2021	FINAL	5-pillar regulatory roadmap
GMLP Guiding Principles (FDA/Health Canada/MHRA)	Oct 2021	FINAL	10 international GMLP principles
Marketing Submission Recommendations for AI/ML SaMD	Apr 2023	DRAFT	Practical submission guidance; PCCP details
Transparency for ML-Enabled Medical Devices	Oct 2023	DRAFT	Labeling requirements for AI devices
AI-Enabled Device Software Functions: Lifecycle Management	Dec 2023	DRAFT	Full lifecycle approach for AI/ML devices
Cybersecurity in Medical Devices	Sept 2023	FINAL	Cybersecurity requirements for all software devices

6. Good Machine Learning Practice (GMLP) — 10 Principles

Co-developed by FDA, Health Canada, and UK MHRA (October 2021). These principles apply across the full AI device development lifecycle.

- 1

Multi-disciplinary expertise throughout the total product lifecycle (clinical, data science, regulatory)
- 2

Good software engineering and security practices integrated from the start
- 3

Clinical study participants and datasets representative of the intended patient population
- 4

Training data independent from test sets — no data leakage between splits
- 5

Reference datasets selected using best available methods for the clinical context
- 6

Model designed to ensure performance for the intended clinical use and patient population
- 7

Focus on the needs of the patient, caregiver, and healthcare provider in design
- 8

Enhance explainability to clinical users — outputs interpretable and actionable
- 9

Deployed models perform as intended in real-world conditions — monitor continuously
- 10

Risks from AI/ML addressed proportionally throughout the device lifecycle

7. Submission Requirements for AI Devices

Technical Documentation (510(k) / De Novo / PMA)

Category	Required Elements
Algorithm Description	Architecture, type (supervised/unsupervised/RL), training methodology, version control
Dataset Characteristics	Size, demographics, geographic origin, inclusion/exclusion criteria, source institutions
Data Management	Preprocessing, augmentation, labeling methodology, inter-rater variability/agreement stats
Train/Val/Test Split	Must be independent; no data leakage; test set held out until final evaluation
Performance Metrics	Sensitivity, specificity, AUC, F1, PPV, NPV as appropriate for clinical use
Subgroup Analysis	Performance across age, sex, race/ethnicity, relevant clinical subgroups
Uncertainty Quantification	Confidence scores, failure modes, out-of-distribution detection
Cybersecurity	Per FDA Sept 2023 cybersecurity guidance — threat modeling, SBOM, patch plan

AI-Specific Labeling Requirements

Per FDA Draft Guidance (Oct 2023), AI device labels must clearly communicate:

Labeling Element	Requirement
Intended use	Specific to AI outputs — what the algorithm predicts/detects/classifies
AI output description	What the output means clinically; scale, confidence, thresholds
Limitations	Known failure modes, populations where performance may differ
Human oversight	Instructions for clinical supervision of AI decisions
Training data scope	Population characteristics that may affect generalizability

8. Post-Market Requirements

Requirement	Details	Applicability
Real-World Performance Monitoring	Monitor AI performance post-deployment; significant degradation = recall/FSCA trigger	All AI devices
Post-Market Surveillance (PMS)	21 CFR Part 822 — mandatory surveillance for Class II/III; AI-specific: track distribution shift, demographic performance changes	Class II & III
MDR — Malfunction Reporting	AI failures causing/contributing to serious injury/death must be reported within 30 days (5 days if urgent)	All device classes
PCCP Tracking	Manufacturers must document and track all PCCP-authorized algorithm updates; deviations require new submission	Adaptive AI devices
Annual Reports	PMA holders must file annual reports on performance, complaints, design changes	PMA (Class III) only

9. Recent Developments (2023–2025)

Development	Date	Impact
Executive Order on AI	Oct 2023	Directed HHS/FDA to develop AI healthcare standards within 365 days; elevated AI to national policy priority
FDA 2024 AI Action Plan Update	2024	Addresses foundation models and generative AI; builds on 2021 plan with focus on LLM-based medical tools
CDRH AI Strategic Plan	2024	10 committed actions: bias mitigation, transparency enforcement, GMLP standards, DHCoE expansion
VALID Act (proposed)	Proposed 2023	Legislation for separate AI diagnostics framework — not yet passed as of early 2025
International Harmonization	Ongoing	FDA aligning with EU AI Act (risk-based), IMDRF SaMD framework, and G7 AI safety standards
Generative AI / LLM Devices	2024–2025	FDA developing new framework for clinical decision support tools using LLMs; increased scrutiny on explainability

Registration Pathway Decision Tree

Q1: Is your AI software intended for medical purposes (diagnosis, treatment, monitoring, prevention)?

↳ YES → **Q2:** Is it a medical device under 21 CFR? (not excluded by 21st Century Cures Act)

↳ YES → **Q3:** What is the risk class?

- └─ **Class I** → General controls (often exempt from 510(k))
- └─ **Class II + predicate exists** → 510(k) Premarket Notification
- └─ **Class II + no predicate** → De Novo Classification Request
- └─ **Class III** → Premarket Approval (PMA)

↳ **Q4:** Does the algorithm adapt/change post-deployment? **YES** → PCCP required

10. References

All references are official FDA, government, or international regulatory body sources.

#	Document / Source	Year	URL
1	FDA — AI/ML Action Plan	2021	https://www.fda.gov/media/145022/download
2	FDA — Proposed Regulatory Framework for AI/ML SaMD	2019	https://www.fda.gov/media/122535/download
3	FDA — Marketing Submission Recommendations for AI/ML SaMD (Draft)	2023	https://www.fda.gov/media/166703/download
4	FDA — Transparency for ML-Enabled Devices (Draft)	2023	https://www.fda.gov/media/173971/download
5	FDA — Lifecycle Management for AI-Enabled Device Software (Draft)	2023	https://www.fda.gov/media/174185/download
6	FDA/Health Canada/MHRA — Good Machine Learning Practice (GMLP)	2021	https://www.fda.gov/medical-devices/software-medical-device-samd/good-machine-learning-practice-medical-device-development-guiding-principles
7	IMDRF — SaMD: Clinical Evaluation (N41)	2017	https://www.imdrf.org/documents/software-medical-device-samd-clinical-evaluation
8	FDA — Digital Health Policy Navigator	Ongoing	https://www.fda.gov/medical-devices/digital-health-center-excellence/digital-health-policy-navigator
9	FDA — Predetermined Change Control Plans for AI/ML SaMD	2023	https://www.fda.gov/regulatory-information/search-fda-guidance-documents/predetermined-change-control-plan-machine-learning-enabled-device-software-functions
10	FDA — 510(k) Premarket Notification Overview	Ongoing	https://www.fda.gov/medical-devices/premarket-submissions-selecting-and-preparing-correct-submission/premarket-notification-510k
11	FDA — De Novo Classification Request	Ongoing	https://www.fda.gov/medical-devices/premarket-submissions-selecting-and-preparing-correct-submission/de-novo-classification-request
12	FDA — Breakthrough Device Designation	Ongoing	https://www.fda.gov/patients/fast-track-breakthrough-therapy-accelerated-approval-priority-review/breakthrough-therapy
13	FDA — AI/ML-Enabled Medical Devices Tracker (CDRH)	Ongoing	https://www.fda.gov/medical-devices/software-medical-device-samd/artificial-intelligence-and-machine-learning-ai-ml-enabled-medical-devices
14	White House — Executive Order on AI (Oct 2023)	2023	https://www.whitehouse.gov/briefing-room/presidential-actions/2023/10/30/executive-order-on-the-safe-secure-and-trustworthy-development-and-use-of-artificial-intelligence/
15	FDA — Cybersecurity in Medical Devices	2023	https://www.fda.gov/regulatory-information/search-fda-guidance-documents/cybersecurity-medical-devices-quality-system-considerations-and-content-premarket-submissions
16	21 CFR Part 820 — Quality System Regulation	—	https://www.ecfr.gov/current/title-21/chapter-I/subchapter-H/part-820
17	21 CFR Part 822 — Postmarket Surveillance	—	https://www.ecfr.gov/current/title-21/chapter-I/subchapter-H/part-822
18	FDA — Digital Health Center of Excellence (DHCoe)	Ongoing	https://www.fda.gov/medical-devices/digital-health-center-excellence

Disclaimer: This report is based on FDA guidance and regulatory knowledge through early 2025. The AI medical device regulatory landscape evolves rapidly — always verify against the latest FDA guidance at [fda.gov](https://www.fda.gov) before filing submissions. All URLs reference official FDA/government sources.