Approaches for managing changes for AI-enabled devices

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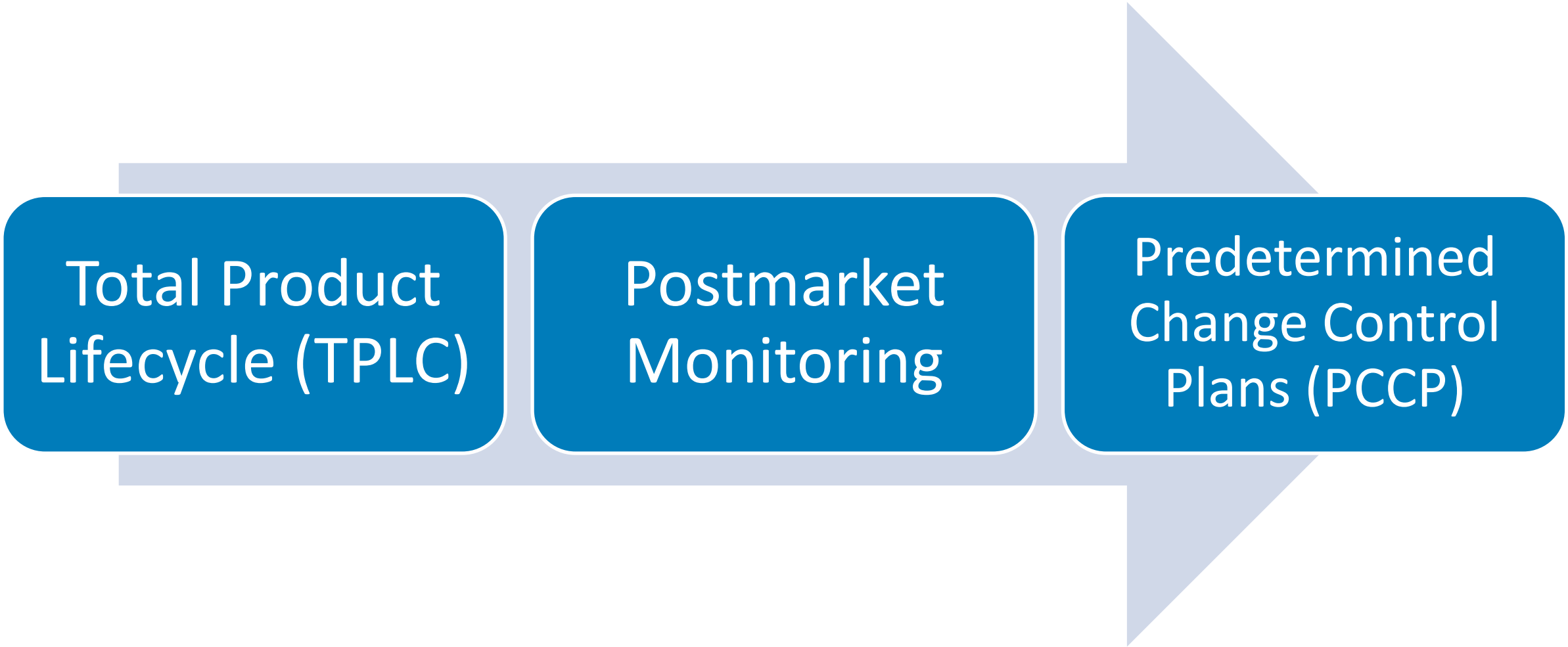
Today's discussion



Total Product Lifecycle Approach to AI

"It is becoming increasingly evident that AI performance should be monitored in the environment in which it is being used"

Warraich HJ, Tazbaz T, Califf RM. FDA Perspective on the Regulation of Artificial Intelligence in Health Care and Biomedicine. *JAMA.* Published online October 15, 2024. doi:10.1001/jama.2024.21451

Internationally Harmonized GMLP Guiding Principles

- **Good Machine Learning Practice (GMLP)** are accepted practices in AI/ML algorithm design, development, training, and testing
- GMLP facilitate the development and assessment of high quality AI/ML-enabled technologies
- US FDA, MHRA (UK) and Health Canada issued 10 Guiding Principles to help inform the development of GMLP
- These 10 principles are intended to promote global harmonization and encourage broad stakeholder engagement

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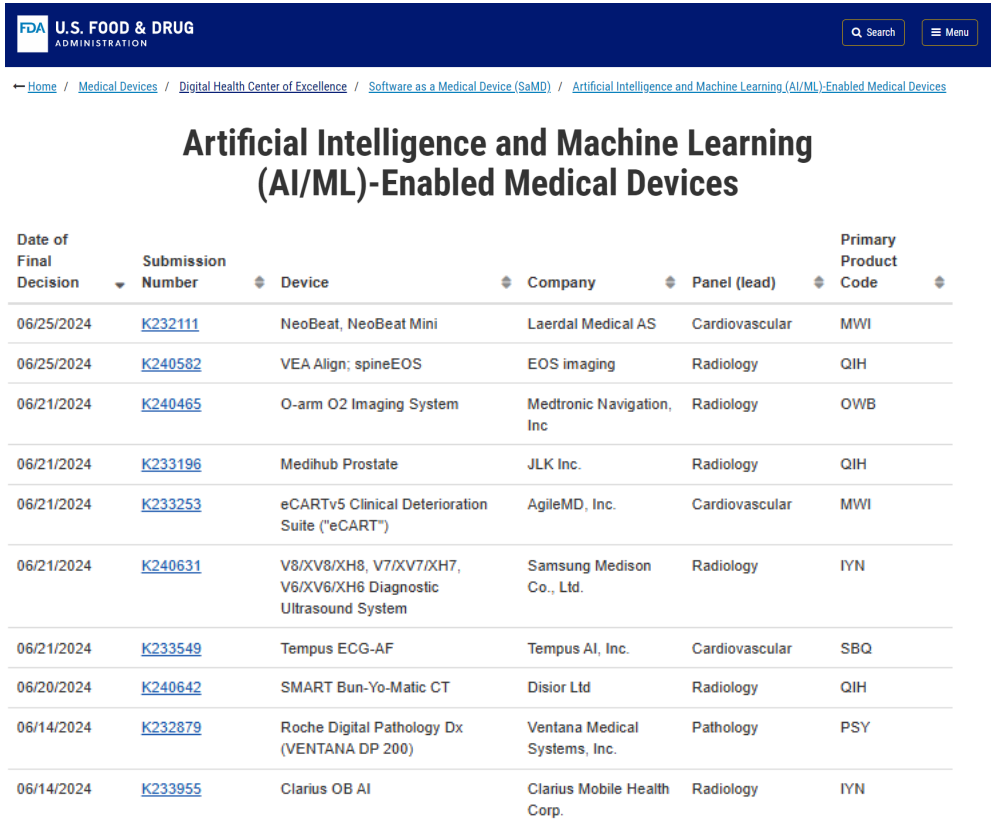
Good Machine Learning Practice for Medical Device Development: Guiding Principles	
Multi-Disciplinary Expertise are Leveraged Throughout the Total Product Life Cycle	Good Software Engineering and Security Practices are Implemented
Clinical Study Participants and Data Sets are Representative of the Intended 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

Learning from AI Device Authorizations



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

Date of Final Decision	Submission Number	Device	Company	Panel (lead)	Primary Product Code
06/25/2024	K232111	NeoBeat, NeoBeat Mini	Laerdal Medical AS	Cardiovascular	MWI
06/25/2024	K240582	VEA Align; spineEOS	EOS imaging	Radiology	QIH
06/21/2024	K240465	O-arm O2 Imaging System	Medtronic Navigation, Inc	Radiology	OWB
06/21/2024	K233196	Medihub Prostate	JLK Inc.	Radiology	QIH
06/21/2024	K233253	eCARTv5 Clinical Deterioration Suite ("eCART")	AgileMD, Inc.	Cardiovascular	MWI
06/21/2024	K240631	V8/XV8/XH8, V7/XV7/XH7, V6/XV6/XH6 Diagnostic Ultrasound System	Samsung Medison Co., Ltd.	Radiology	IYN
06/21/2024	K233549	Tempus ECG-AF	Tempus AI, Inc.	Cardiovascular	SBQ
06/20/2024	K240642	SMART Bun-Yo-Matic CT	Disior Ltd	Radiology	QIH
06/14/2024	K232879	Roche Digital Pathology Dx (VENTANA DP 200)	Ventana Medical Systems, Inc.	Pathology	PSY
06/14/2024	K233955	Clarius OB AI	Clarius Mobile Health Corp.	Radiology	IYN

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

Recent authorization example: AI/ML-enabled Sepsis ImmunoScore

- Identifies patients at risk for having or developing sepsis
  - Uses data from the patient's electronic health record in conjunction with other laboratory findings and clinical assessments to aid in the risk assessment for presence of or progression to sepsis within 24 hours of assessing a patient who has been admitted to the emergency department or hospital and meets certain other criteria. Should not be used as the sole basis to determine the presence of sepsis.

- Establishes specific premarket and postmarket requirements for this device type, such as:
  - Software validation and clinical performance testing before authorized for marketing
  - **Development and implementation of a post-market performance management plan**

Special controls – performance monitoring

- Technological characteristics of GenAI may sometimes introduce new or different risks for a particular GenAI-enabled product, which raises new questions of safety and effectiveness

- De Novo may be necessary → establish new device type and special controls, as appropriate

- FDA may require special controls unique to GenAI-enabled devices when needed to provide reasonable assurance of safety and effectiveness of the device. Such special controls could include requirements for postmarket monitoring, such as the need for a performance monitoring plan

Predetermined Change Control Plans for Devices: Section 515C of the FD&C Act

2022 Omnibus Appropriations Bill

Added section 515C to the FD&C Act so that changes to a device consistent with an approved predetermined change control plan do not require a supplemental application.

Scope

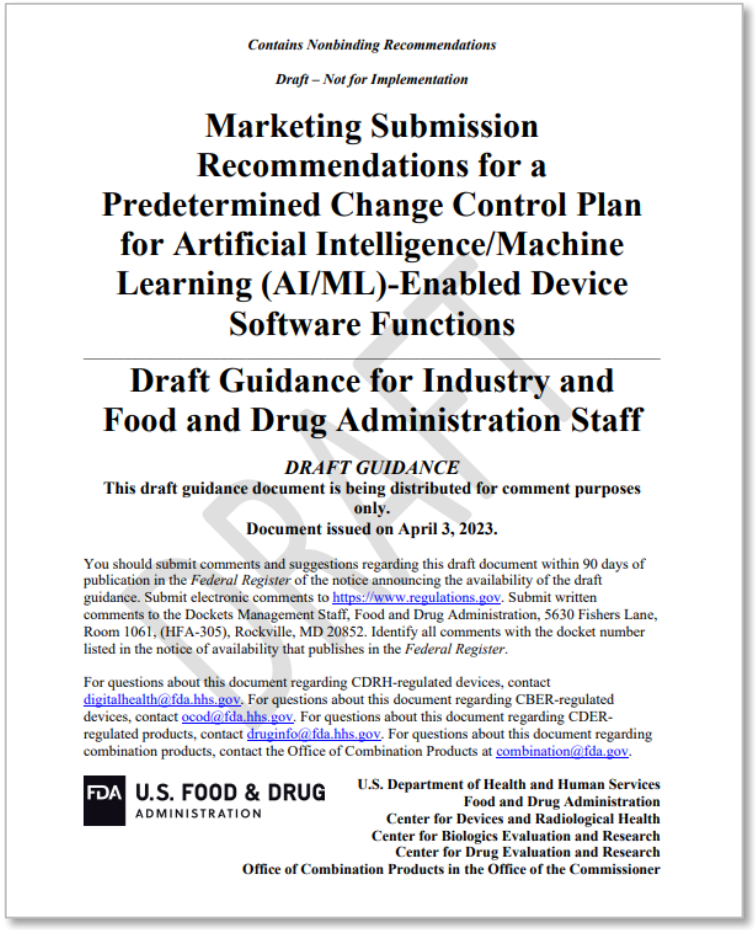
This provision applies to all devices—it is not specific to software or AI/ML-enabled devices. It applies to both premarket approvals and 510(k) applications.

Predetermined Change Control Plans

PCCPs are planned changes that may be made to the device (and that would otherwise require a supplemental application) if the device remains safe and effective without any change.

- ✓ 515C is in effect and self-executing
- ✓ Manufacturers may submit, and FDA may approve or clear, a PCCP for a device at this time

Promoting Development of Safe and Effective AI/ML-Enabled Devices



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.

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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 draft guidance:

- Proposes a science-based approach to put safe and effective advancements in hands of health care providers and users faster. The Predetermined Change Control Plan (PCCP):
  - Helps to increase pace of medical device innovation
  - Is informed by FDA's experience in regulating AI/ML-enabled devices

Components of PCCPs

Description of Modifications

"What" a manufacturer intends the algorithm to become as it learns

- Identifies specific, planned modifications to AI-DSF that the manufacturer intends to implement
- Includes the specifications for the characteristics and performance of the planned modifications to the AI-DSF

Modification Protocol

"How" the algorithm will learn/change while remaining safe and effective

- Describes methods that will be followed when developing, validating, and implementing the modifications to ensure the device remains safe and effective
- Methods described in Modification Protocol should be consistent with and support the modifications outlined in Description of Modifications

Impact Assessment

Describes modifications' benefits and risks, and how risks are mitigated

- Assesses benefits and risks of each individual modification, as well as collective impact of modifications, when implementing a PCCP
- Discusses how activities proposed within Modification Protocol mitigate identified risks to continue to reasonably ensure the safety and effectiveness of the device

Predetermined Change Control Plan

Description of Modifications

Provides a detailed description (e.g., changes to device characteristics, performance) of each planned modification to an AI-DSF that the manufacturer intends to implement

- Identify specific modifications that can be verified and validated
- Present modifications at a level of detail that permits understanding of specific AI-DSF changes
- State whether planned modifications will be implemented manually or automatically
- Specify if proposed modifications will be implemented globally or locally

Modifications Appropriate for a PCCP

- ✓ Are to maintain or improve the safety or effectiveness of the device
- ✓ Are specific
- ✓ Able to be verified and validated
- ✓ Maintain the device within the device's intended use

Modification Protocol

Describes the methods that will be followed when developing, validating, and implementing modifications

- Should include the verification and validation activities, including pre-defined acceptance criteria, that will support those modifications while assuring the device remains safe and effective
- Methods described in Modification Protocol should be **consistent with and support** modifications outlined in Description of Modifications
- Includes a description of how proposed methods are similar to, or are different from, methods used elsewhere in marketing submission

Components of Modification Protocol

(1) Data Management	(2) Re-Training	(3) Performance Evaluation	(4) Update Procedures
• Collection Protocols • Assurance of Data Quality • Reference Standard Determination • Sequestration of Test Data Sets	• Re-training Objectives and Focus • Re-training Implementation	• Triggers to Initiate Performance Evaluation • Assessment Metrics and Elements • Statistical Analysis Plans • Performance Targets • Additional Testing Needs	• Software Verification and Validation • Update Implementation (When/How) • Communication and Transparency to Users • Device Monitoring Plan

From Appendix A

Impact Assessment

Documentation for an Impact Assessment provided to the Agency in a marketing submission containing a PCCP should:

1. Compare version of device with each modification implemented individually to version of device without any modifications implemented
2. Discuss benefits and risks, including risks of harm and unintended bias, of each individual modification
3. Discuss how verification and validation activities proposed within Modification Protocol continue to reasonably ensure safety and effectiveness of device
4. Discuss how implementation of one modification impacts implementation of another
5. Discuss cumulative impact of implementing all modifications

Labeling Related to PCCPs

FDA recommends that the labeling related to a PCCP be updated with the following information to help make users aware of modifications that have been implemented via the PCCP that impact device use:

A **description of the implemented modifications**, including a summary of current device performance, a description of the relevant data (training, tuning, and testing data) as applicable, associated inputs/outputs, validation requirements, and related evidence;	A description of **how the modifications were implemented**;	A description of **how users will be informed** of implemented modifications, including, for example, updated instructions for use or a version history

Note that, FDA may require that a device with an authorized PCCP include labeling required for safe and effective use of the device as such devices changed pursuant to such a plan
(See sections 515C(a)(3), 515C(b)(3), and 513(f)(2) of the FD&C Act)

Public Decision Summary Content Related to PCCPs

FDA recommends public-facing documents include a summary of the following information related to a PCCP:

- Planned modifications;
- Testing methods;
- Validation activities and performance requirements to be met in order for modifications to be implemented; and
- Means by which users will be informed of device modifications implemented in accordance with the authorized PCCP

Considerations for PCCPs for Adaptive Algorithms

- FDA would likely consider:
  - How specific the modifications can be for an adaptive algorithm
  - What boundaries or guardrails are established in the PCCP to define the range of automatic updates
  - How post-market performance will be monitored over time to assure device performance is maintained or improved
    - Monitoring across multiple sites, allowing for local, site-specific adaptations
  - How labeling will be updated when modifications are implemented automatically to inform users
  - Appropriate notification requirements if the device does not function as intended pursuant with the PCCP


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