U.S. FOOD & DRUG ADMINISTRATION

Welcome To Today's Webinar

Thanks for joining us!

We'll get started in a few minutes

Today's Topic:

Marketing Submission Recommendations for a Predetermined Change Control Plan for Artificial Intelligence-Enabled Device Software Functions

January 14, 2025

Marketing Submission Recommendations for a Predetermined Change Control Plan for Artificial Intelligence-Enabled Device Software Functions

Jessica Paulsen
Associate Director for Digital Health
Office of Product Evaluation and Quality

B.Y. MiRa Jacobs, PhD
Division Director
Division of Digital Health Policy
Digital Health Center of Excellence

Ayobami Adebowale, M.Eng
Policy Analyst
Division of Digital Health Policy
Digital Health Center of Excellence

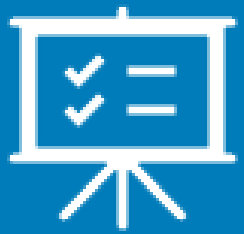
Center for Devices and Radiological Health
U.S. Food and Drug Administration

Jessica Paulsen
Associate Director for Digital Health
Office of Product Evaluation and Quality

Final Guidance

- **Marketing Submission Recommendations for a Predetermined Change Control Plan for Artificial Intelligence-Enabled Device Software Functions**
  - www.fda.gov/regulatory-information/search-fda-guidance-documents/marketing-submission-recommendations-predetermined-change-control-plan-artificial-intelligence

Learning Objectives



- ✓ Summarize comments received and explain changes from the draft to the final guidance
- ✓ Describe the scope and policy of the final guidance
- ✓ Describe the recommendations for information to be included in a Predetermined Change Control Plan (PCCP) in a marketing submission for an Artificial Intelligence (AI)-enabled device
- ✓ Explain FDA's policy on the types of modifications that may be included in a PCCP for Artificial Intelligence-Enabled Device Software Functions (AI-DSFs)

FDA's Collaborative Patient-Centered Approach to "AI/ML-Enabled Devices"

2019

Discussion Paper

Described concepts for a potential regulatory framework for modifications to AI/ML-enabled medical device software to assure their safety and effectiveness, including **pre-specification of software changes to enable rapid improvement of software products**

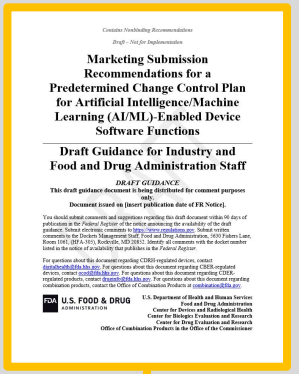
2021

Action Plan

Holistic, patient-centered strategic approach to AI/ML-enabled devices that promotes health equity, including aims to **update the proposed regulatory framework** and **foster a patient-centered approach, including transparency to users**

2023

Draft Guidance



Proposed, **least burdensome** approach to support safe, iterative improvement through modifications to an AI/ML-enabled device

“Predetermined Change Control Plans for Devices” in section 515C of the FD&C Act

2022 Omnibus Appropriations Bill

Added *section 515C to the FD&C Act,* which has provisions regarding PCCPs for devices that would otherwise require a PMA supplement or a new 510(k)

Scope*

This provision applies to all device types—it is not specific to software or AI/ML-enabled devices. It applies to both PMA and 510(k). This provision is consistent with what FDA has been describing for several years in both our AI/ML Action Plan and Discussion Paper

Predetermined Change Control Plans

PCCPs describe planned changes that may be made to the device (and that would otherwise require a PMA supplement or 510(k) under section 515C of the FD&C Act) if the device remains safe and effective without any change

**Predetermined Change Control Plans for Medical Devices - Draft Guidance August 2024*

Summary of Comments Received and Changes to Guidance

Summary of Comments received in the Docket

We received requests for clarification throughout the guidance, including:

- **The scope of guidance**, including applicability to combination products and devices that are not enabled by AI
- **Terminology** included in the draft (i.e., training, tuning, and test data)
- Information to include on the PCCP in the **device's labeling and publicly available summaries**
- **Submission types** to establish and modify a PCCP for a device
- Implementation of a modification to a device consistent with **an authorized PCCP**
- **Modification types** that may be appropriate for inclusion in a PCCP
- **Post-market surveillance**

We also received requests to include **additional examples**

Summary of Changes from Draft to Final

- Clarified the guidance applies **to the device constituent part of device-led combination products**
  - Included an example AI-DSF scenario employing a PCCP for a device-led combination product
- Specified marketing submission types for **establishing and modifying PCCPs**
- Provided recommendations on **information** that should be included **about a PCCP in device labeling and public-facing documents**
- Updated **Terminology and Definitions**
- Clarified **post-market surveillance** recommendations
- Provided clarification regarding **PCCP implementation**, version control, and maintenance
- Revised recommendations on **modification types** that may be appropriate for inclusion in a PCCP

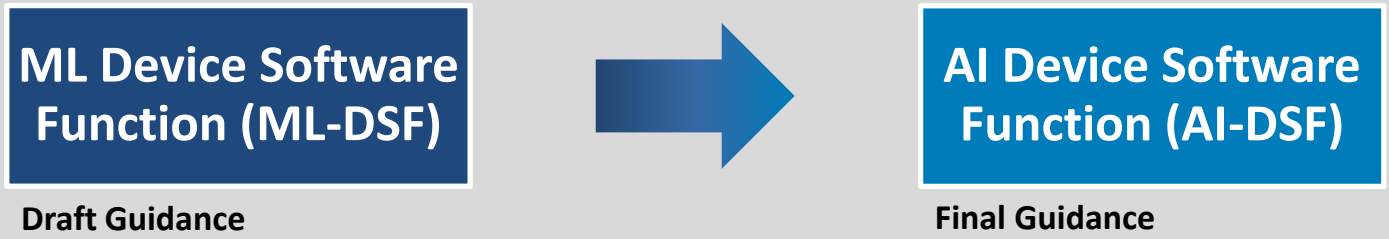
From draft to final

Specific to the AI PCCP Guidance

TIP

Update

Definitions: AI, ML, and AI-DSF



- **Artificial Intelligence (AI):** A machine-based system that can, for a given set of human-defined objectives, make predictions, recommendations, or decisions influencing real or virtual environments
- **Machine Learning (ML):** A set of techniques that can be used to train AI algorithms to improve performance at a task based on data
- **Artificial Intelligence-Enabled Device Software Function (AI-DSF):** A device software function that implements an AI model

Definitions: PCCP

- **Predetermined Change Control Plan (PCCP):** Documentation describing what modifications will be made to a device and how the modifications will be assessed. The PCCP should include:
  - Description of Modifications
  - Modification Protocol
  - Impact Assessment

- **Authorized Predetermined Change Control Plan:** A PCCP that has been reviewed and established through a device marketing authorization. An authorized PCCP is a technological characteristic of the authorized device with which it was established.

Scope of Final Guidance

AI PCCP

- Applies to **Artificial Intelligence-Enabled Device Software** functions (AI-DSFs) that a manufacturer intends to modify over time
- Describes recommendations on information to be included in a **PCCP provided as part of a marketing submission for an AI-enabled device**
  - NOTE: PCCPs remain an optional mechanism

Update

- Generally, the recommendations in this guidance **apply to the device constituent part of device-led combination products** when the device constituent part **includes an AI-DSF**
  - If a modification to the AI-DSF in a PCCP impacts the drug or biologic constituent part, we highly encourage early engagement with FDA

Scope of Final Guidance

- **NOT** intended to delineate ALL types of modifications the Agency would consider acceptable in a PCCP
- **NOT** intended to provide a complete description of what may be necessary to include in a marketing submission for an AI-DSF
- FDA review division determines whether the scope of modifications is appropriate for inclusion in a PCCP and what evidence and information would ensure that the AI-DSF under that PCCP remains safe and effective

Ayobami Adebowale, M.Eng.
Policy Analyst
Division of Digital Health Policy
Digital Health Center of Excellence

Policy for PCCPs

An authorized PCCP specifies planned modifications that, if not included in a PCCP, could otherwise require a new marketing submission*

The modifications can be implemented to the AI-DSF without triggering the need for a new marketing submission

Modifications made to an AI-DSF that are not specified in the authorized PCCP could require a new marketing submission*

*Note: Pursuant to 21 CFR 807.81(a)(3) and 21 CFR 814.39(a), and in accordance with the "Modifications" guidances. For a list of the "Modifications" guidances, please see the Resources slide.

Recommended 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

Identifying a PCCP in a Marketing Submission

In a marketing submission the PCCP should:	Be a standalone section with a title and version number
	Be noted in the cover letter and listed in the table of contents as “Predetermined Change Control Plan”
	Be discussed as part of the device description, labeling, and other relevant sections related to safety and effectiveness or substantial equivalence

Update

Establishing a PCCP

- A PCCP **is included in a marketing submission for a device and established as part of that authorization***
- An "authorized PCCP" is one that has been reviewed and established through the device marketing authorization

PMA
- Original PMA submission
- Modular PMA submission
- 180-Day PMA supplement
- Panel Track PMA supplement
- Real-Time PMA supplement

510(k)
- Abbreviated 510(k)
- Traditional 510(k)

In making a determination of substantial equivalence where the predicate device was authorized with a PCCP, the subject device must be compared to the version of the predicate device cleared or approved prior to changes made under the PCCP

De Novo
- Original De Novo Submission

***The term "authorization" is used to include clearance of a 510(k), granting of a De Novo, or approval of PMA**

Update

Modifying a Previously Authorized PCCP

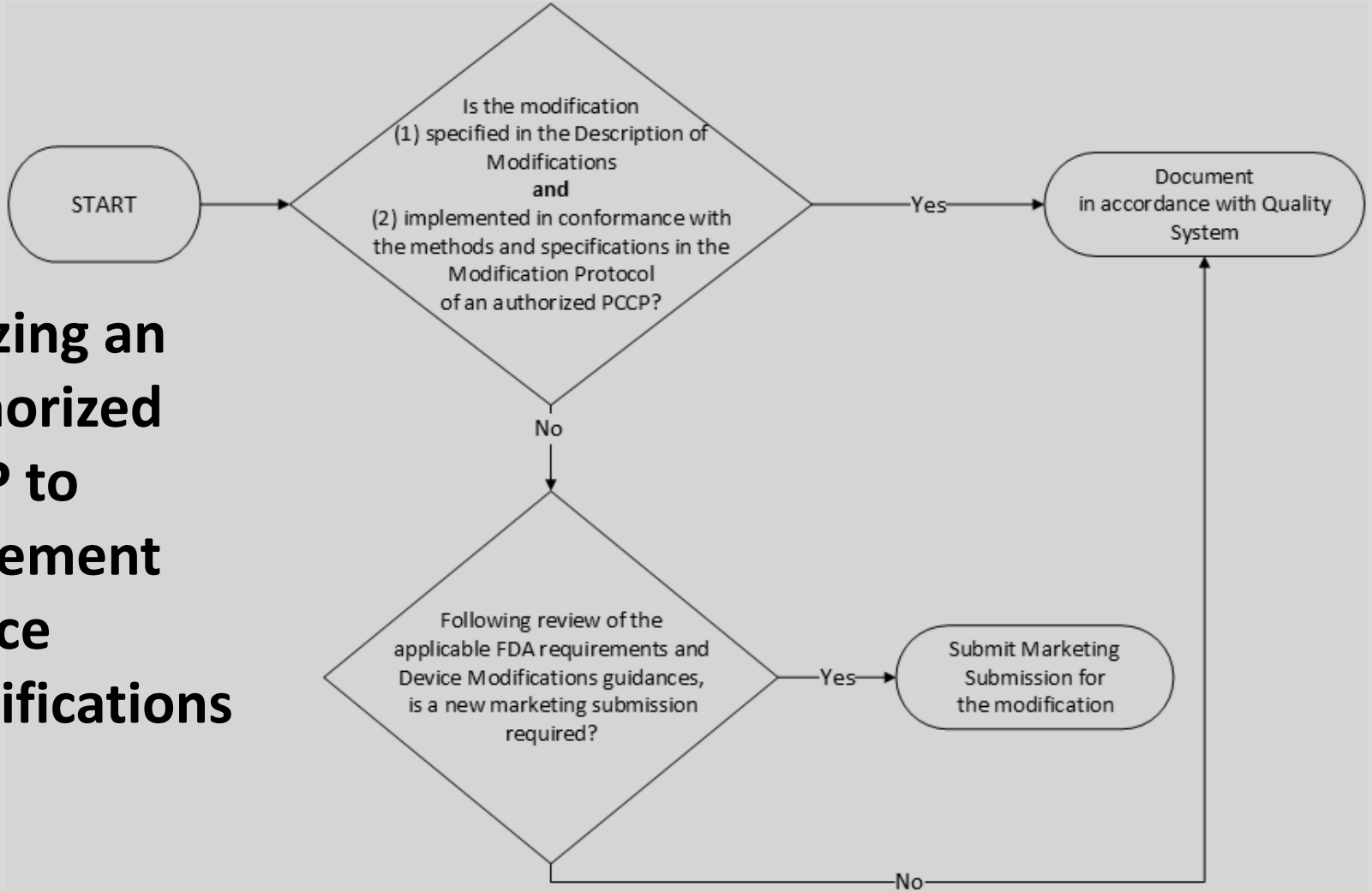
- Because a **modification to the PCCP** will generally significantly affect the safety or effectiveness of the device, generally, **a new marketing submission is required**
- To **modify a PCCP for a previously authorized device with a PCCP**, the marketing submission must include the appropriate marketing submission requirements for the device and a proposed PCCP
  - An authorized PCCP is applicable only to the version of the authorized device with which it was established

510(k)	**PMA**
Traditional 510(k)	180-Day PMA supplement
Abbreviated 510(k)	Panel Track PMA supplement
Special 510(k)*	Real-Time PMA supplement

*The Special 510(k) pathway to modify a PCCP may be appropriate when modifications to a PCCP are changes to the manufacturer's own device and PCCP and where well-established methods are available to evaluate the change

TIP: Provide a summary of changes to the authorized PCCP, and where applicable, a tracked changes version compared to the authorized PCCP!

Utilizing an Authorized PCCP to Implement Device 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:

AI PCCP

A **description of the implemented modifications**, including a summary of current device performance, a description of the relevant data (training, tuning, and test 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

Update

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

TIP: Include description of the PCCP in sufficient detail to support transparency to users regarding the safety and effectiveness of the device!

Update

Version Control of a PCCP

- FDA recommends submitting a copy of the proposed PCCP with a title and version number
- FDA expects that reviews of PCCPs will be very interactive; FDA and the manufacturer should work together to revise the PCCP utilizing existing processes (e.g., interactive review, deficiency letters)
  - ✓ PCCP successfully revised
    - If a PCCP is revised, a final, revised version of the PCCP should be submitted as clean copy, with a title and current version number
    - FDA authorizes the PCCP as part of the marketing authorization of a device; the PCCP will be referenced in the device's letter of authorization, including the PCCP's title and version number
  - ✘ PCCP is not successfully revised
    - If deficiencies with the PCCP remain unresolved, FDA may authorize the device upon withdrawal of the PCCP
- An authorized device will generally have only one authorized PCCP associated with it. However, a PCCP can evolve over time through future marketing submissions, where new versions of the PCCP may be authorized

B.Y. MiRa Jacobs, PhD
Division Director
Division of Digital Health Policy
Digital Health Center of Excellence

Description of Modifications

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

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

AI PCCP

AI PCCP

- 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

TIP: Include only a limited number of modifications that are specific, and that can be verified and validated!

Modifications Appropriate for a PCCP

- Modifications should maintain or improve the safety or effectiveness of the device
- Modifications should be specific and should be able to be verified and validated
- Modifications must maintain the device within the device's intended use

Types of Modifications for a PCCP

Modifications related to **quantitative measures** of AI-DSF performance specifications	Modifications related to **device inputs to, and compatibility** with, the AI-DSF	Certain modifications related to the **device's use and performance**
Example: Improvements to analytical and clinical performance resulting from re-training the AI model based on new data within intended use population from the same type and range of input signal	**Example**: Changes to data type specifications to include new sources of same signal type (such as different makes, models, or versions of a data acquisition system) or limited modifications related to new types of inputs (such as adding/transforming data inputs)	**Example**: Authorization of a device for specific subpopulation within originally indicated population based on re-training on a larger data set for that subpopulation that was not previously available

TIP: Use a Pre-Submission to discuss proposed modifications in a PCCP!

Modification Protocol

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

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

Traceability Table

	Modification Protocol Component			
Modification	Data management practices	Re-training practices	Performance evaluation	Update procedures
Modification #1	Method A (see Section X.A)	Method D (see Section X.D)	Method G (see Section X.G)	Method J (see Section X.J)
Modification #2	Method A (see Section X.A)	Method E (see Section X.E)	Method H (see Section X.H)	Method J (see Section X.J)
Modification #3	Method B (see Section X.B)	Method F (see Section X.F)	Method I (see Section X.I)	Method J (see Section X.J)

TIP: Use a traceability table to clearly delineate which parts of Modification Protocol are applicable to each modification within Description of Modifications!

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

Impact Assessment

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

TIP: Your risk assessment ≠ Impact Assessment in a PCCP. Consider the recommended documentation, and as appropriate, reference your risk assessment!

Impact Assessment

- Should discuss how the individual modifications included in the PCCP impact not only the particular device function, but the overall functionality of the device, including:
  - How they impact other device software functions and/or device hardware
  - For combination products, how they impact the biologic and/or drug constituent part, and the combination product as a whole

Update

Example

Device | *Proposed Modifications* | *Post-Authorization Scenarios*

Optical Imaging System Co-packaged with Imaging Drug

The product is a device-led combination product including an AI-DSF integrated into an imaging system co-packaged with an approved optical imaging drug. The AI-DSF analyzes images in real-time and highlights potential cancerous lesions for further evaluation. The product was authorized with a PCCP.

Example

Device | **Proposed Modifications** | *Post-Authorization Scenarios*

Optical Imaging System Co-packaged with Imaging Drug

The manufacturer would like to train the AI-DSF to improve speed of the lesion detection. The PCCP specifies that the speed of lesion detection can be improved provided that the sensitivity and specificity do not fall below a pre-specified level.

Example

Device | *Proposed Modifications* | **Post-Authorization Scenarios**

Modification Scenario 1

Modification related to device performance, as specified in the PCCP and implemented in accordance with the PCCP

Modification Scenario 2

Modification related to device's use that was not specified in the PCCP

Modification Scenario 1

Modification Scenario

Modification related to device performance, as specified in the PCCP and implemented in accordance with the PCCP

- AI-DSF was retrained using imaging data collected and analyzed in accordance with the Modification Protocol
- Analytical validation demonstrated that the modified AI-DSF resulted in image processing speed improvements of 20%
- Analytical performance of the imaging system with the increased image processing speed was found to be statistically equivalent to the baseline performance of the imaging system, as specified in the Modification Protocol

Because the device modification was specified in the PCCP, and it was implemented in conformance with the PCCP, the device modification would not require a new marketing submission

Manufacturer should document the modification that was specified in PCCP in accordance with their quality system

Modification Scenario 2

Modification Scenario

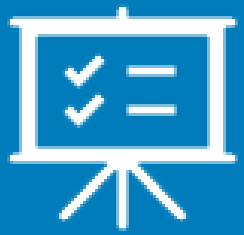
Modification related to the device's use that was <u>not specified in the PCCP</u>

- Manufacturer would like to distribute a new version of the AI-DSF that is used with a modified dosing regimen of the drug
- Modification was not specified in the PCCP

Because this modification was not included in the PCCP, and it could significantly affect the safety or effectiveness of the device, a new marketing submission would be required

Note, recommendations in this guidance do not apply to modifications to the drug or biologic constituent part of device-led combination products

Summary



This final guidance:

- ✓ Describes FDA's approach to PCCPs for AI-DSFs to support their iterative development and improvement over time
- ✓ Explains FDA's recommendations on information to be included in a PCCP provided as part of a marketing submission for an AI-DSF
- ✓ Explains FDA's recommendations of the types of modifications to include in a PCCP for an AI-DSF

Pre-Subs for PCCPs can be helpful!

We encourage manufacturers to engage early with FDA by submitting a Pre-Submission to discuss a proposed PCCP!

Pre-Subs can be a helpful way to obtain feedback on:

- A proposed PCCP for an AI-enabled device prior to submitting a marketing submission
- A proposed submission type for an AI-enabled device and PCCP
- Specific, proposed modifications for an AI-enabled device
  - Automatic and/or local modifications
- Proposed modifications to a PCCP

TIP: Engage with FDA early and often on your PCCP!

Resources

Slide Number	Cited Resource	URL
16	21 CFR 807.81(a)(3)	www.ecfr.gov/current/title-21/chapter-I/subchapter-H/part-807/subpart-E/section-807.81#p-807.81(a)(3)
16	21 CFR 814.39(a)	www.ecfr.gov/current/title-21/chapter-I/subchapter-H/part-814/subpart-B/section-814.39#p-814.39(a)
16	Deciding When to Submit a 510(k) for a Software Change to an Existing Device	www.fda.gov/regulatory-information/search-fda-guidance-documents/deciding-when-submit-510k-software-change-existing-device
16	Deciding When to Submit a 510(k) for a Change to an Existing Device	www.fda.gov/regulatory-information/search-fda-guidance-documents/deciding-when-submit-510k-change-existing-device
16	Modifications to Devices Subject to Premarket Approval (PMA)	www.fda.gov/regulatory-information/search-fda-guidance-documents/modifications-devices-subject-premarket-approval-pma-pma-supplement-decision-making-process

Acronyms

Acronym	Meaning
PCCP	Predetermined Change Control Plan
AI	Artificial Intelligence
ML	Machine Learning
DSF	Device Software Function
AI-DSF	Artificial Intelligence-Enabled Device Software Function
FD&C Act	Federal Food, Drug, and Cosmetic Act
FDORA	Food and Drug Omnibus Reform Act
PMA	Premarket approval
510(k)	Premarket notification
CFR	Code of Federal Regulations


FDA
U.S. FOOD & DRUG
ADMINISTRATION

Additional Panelists

Kathryn Drzewiecki, PhD
Team Lead
Division of Digital Health Policy
Digital Health Center of Excellence

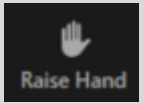
Nicholas Petrick, PhD
Deputy Director
Division of Imaging, Diagnostics, and Software Reliability
Office of Science and Engineering Laboratories

Amir Khan, PhD
Senior Staff Fellow
Imaging Software Team
Office of Radiological Health
Office of Product Evaluation and Quality

Aneesh Deoras
Assistant Director
Cardiac Ablation, Mapping, and Imaging Devices Team
Office of Cardiovascular Devices
Office of Product Evaluation and Quality

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

Let's Take Your Questions

- **To Ask a Question:**
  1. Raise your hand in Zoom 

  2. Moderator will announce your name and invite you to ask your question
  3. Unmute yourself when prompted in Zoom to ask your question

- **When Asking a Question:**
  - Ask one question only
  - Keep question short
  - No questions about specific submissions

- **After Question is Answered:**
  - Mute yourself and lower your hand
  - If you have more questions - raise your hand again

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