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FDA Draft Guidance on Artificial Intelligence/Machine Learning Enabled Device Software Functions & Predetermined Change Control Plans (PCCP'S)

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Date: Oct 27, 2023

Presenter Overview

Monica Montanez - Principal Strategy Consultant

- 25 years in MedTech Regulatory– Past 4 at NAMSA
- Past Experience with Millar Instruments - Cyberonics (now Liva Nova) – CONMED - Generic Medical Devices, Inc - Cochlear and Medtronic.
- With NAMSA, primary work focus with manufacturers on complex submissions for novel devices.
- In-house expert for regulatory software as a medical device (SaMD), Artificial Intelligence (AI) and Machine Learning (ML).
- Master’s of Science in Regulatory Science - School of Pharmacy USC

BACKGROUND – KEY ELEMENTS

- 2019 – FDA published "Proposed Regulatory Framework for Modifications to Artificial Intelligence/Machine Learn (AI/ML) Based Software as a Medical Device (SaMD)
- 2021 – Artificial Intelligence/Machine Learning (AI/ML) Based Software as a Medical Device (SaMD) Action Plan
- 2022 – Food and Drug Omnibus Reform Act of 2022 (FDORA) Section 3308*
- 2023 – Marketing Submission Recommendations for a Predetermined Change Control Plan for Artificial Intelligence/Machine Learning (AI/ML) Enables Device Software Guidance**

*Note: This provision applies to all devices and is not specific to AI/ML-enables devices or software devices

** Note: FDA states the guidance does not intend to provide a complete description of what may be necessary to include in a marketing submission for ML-enables software functions

DEFINITION OF PREDTERMINED CHANGE CONTROL PLAN (PCCP)

Documentation describing what modifications will be made to the ML-DSL and how the modifications will be assessed. This includes:

- Description of Modifications
- Modification Protocol
- Impact Assessment

Note: 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.

DRAFT POLICY FOR PCCP'S

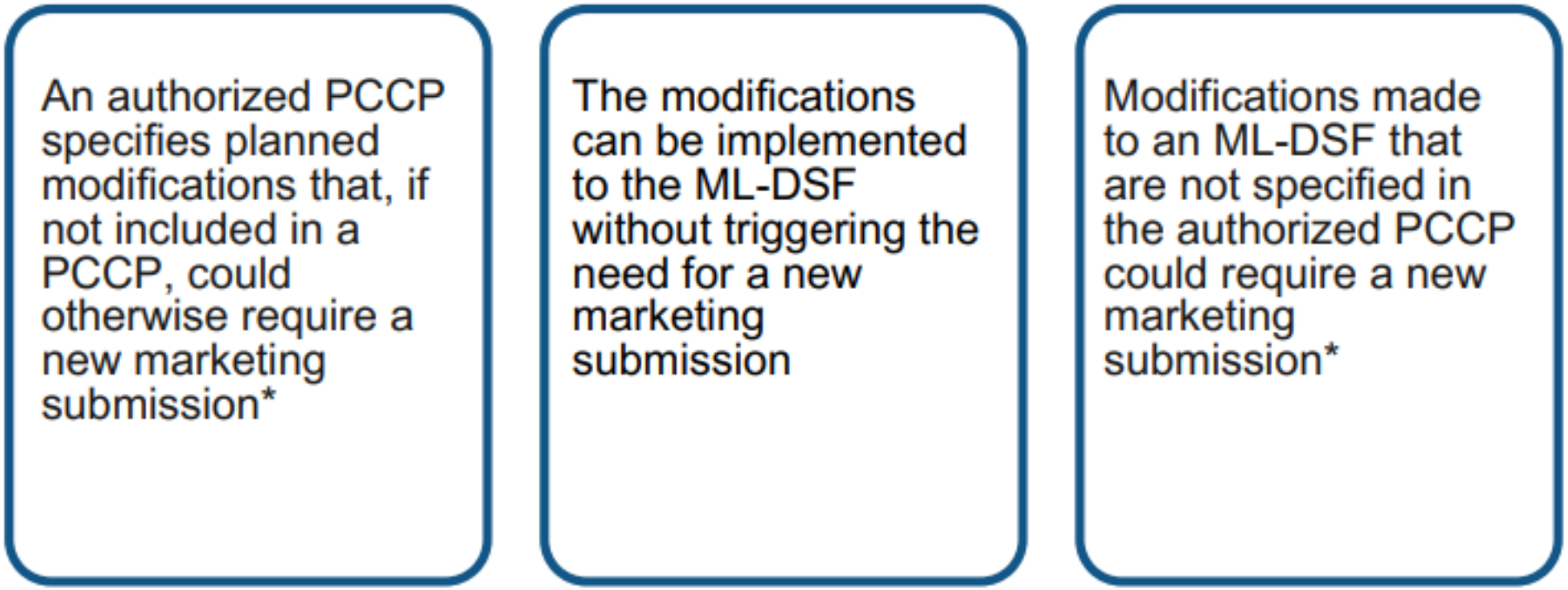


Figure 1: Draft Policy for PCCPs

RECOMMENDED CONTENTS OF PCCP IN SUBMISSION

1) Should be a standalone section
2) Noted in the Cover Letter
3) Listed in the Table of Contents as “Predetermined Change Control Plan”
4) Described in the 510(k) Summary or De Novo Decision Summary; or
5) PMA Summary of Safety and Effectiveness Document (SSED) and approval order
6) Details should be included in sufficient detail to support transparency to users regarding the safety and effectiveness of the device
7) Device Description, labeling and/or relevant sections

INSIDE THE PCCP-COMPARISION OF 2019 DISCUSSION PAPER TO DRAFT FDA GUIDANCE

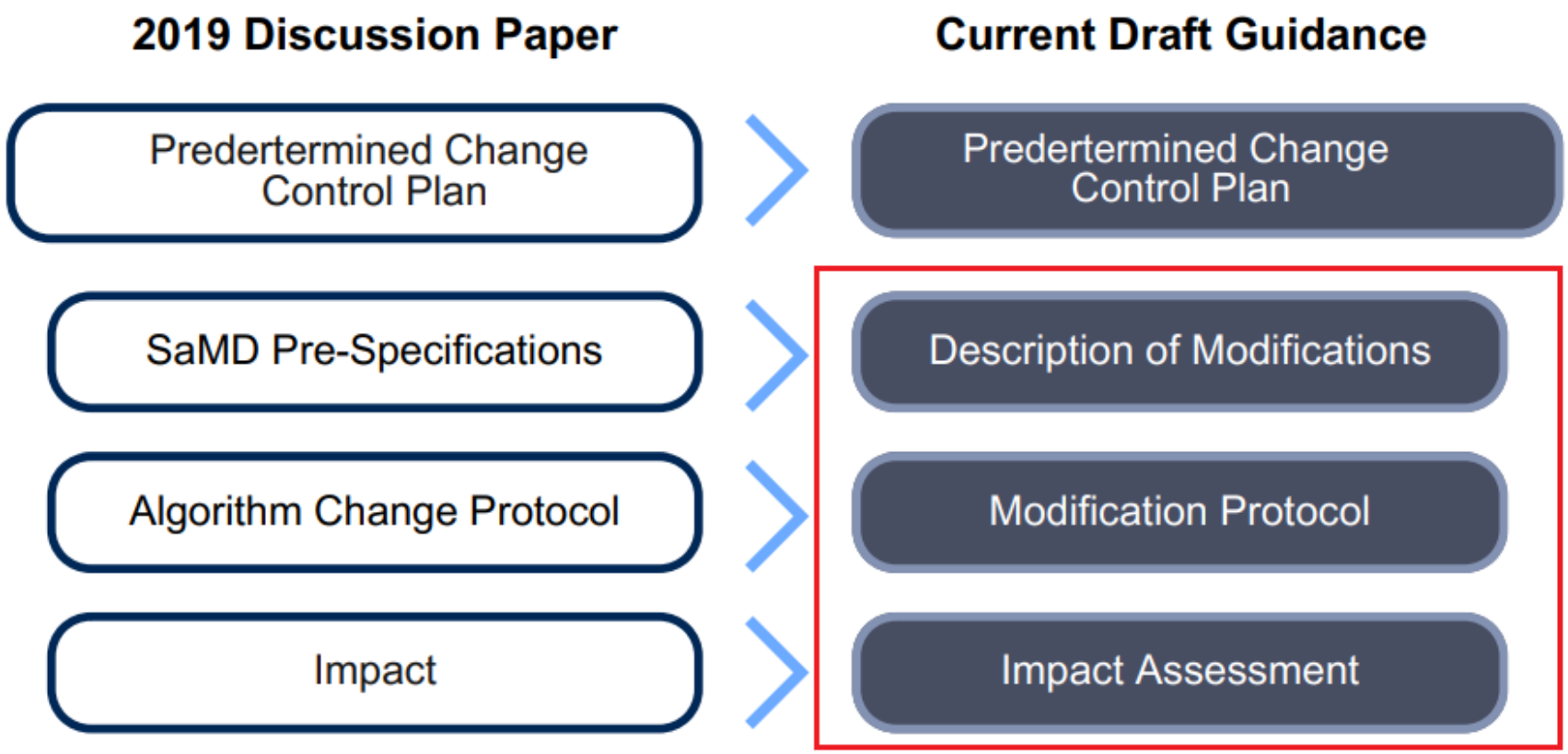


Figure 2: PCCP Term Mapping

DESCRIPTION OF THE MODIFICATION –PART 1 “THE WHAT”

Is the “what” a manufacturer intends the algorithm to become as it learns. The description of modifications should include:

- A detailed description of each planned modification to an ML_DSL
- Describe changes to the device characteristics and performance resulting from implementation of modifications

MODIFICATION PROTOCOL – PART 2

Figure 3: Elements of a Modifications Protocol

IMPACT ASSESSMENT – PART 3

Describes:

- Benefits and Risks and how risks are mitigated for each individual modification
- Collective impact of modifications
- Description of modifications

Should Include:

- Compare version of device with each modification implemented to version of device without any modifications implemented
- Discuss benefits and risks of each individual modification
- Discuss how activities proposed within the Modification Protocol continue to reasonable ensure safety and effectiveness of the device
- Discuss how implementation of one modification impacts implementation of another
- Discuss the collective impact of implementing all modifications

PCCP WITH MULTIPLE MODIFICATIONS

Traceability Between the Description of Modifications and the Modification Protocol

The PCCP should clearly delineate which parts of the Modification Protocol are applicable to each modification within the Description of Modifications. For a PCCP with multiple modifications, this may be accomplished through a traceability table. A sample traceability table is provided in **Table 1**.

	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)

Table 1: Example of Description of Modifications to Modification Protocol Traceability Table

MODIFICATION SCENARIO 1

Change: Does a Modification in input, as specified in the PCCP and implemented in accordance with the PCCP require a new marketing authorization? YES or NO?

Details:

- Analytical validation demonstrated the ML-DSF can be deployed on two additional smartphones that meet the minimum specifications provided in the PCCP. The analytical performance using the new image acquisition systems was found to be statistically equivalent to the baseline performance
- Labeling was updated to reflect new ML-DSF compatibility with additional smartphones and communications updates on device compatibility were also provided.

MODIFICATION SCENARIO 1- RESPONSE

Change: Does a Modification in input, as specified in the PCCP and implemented in accordance with the PCCP require a new marketing authorization?

Answer: **No.** A new marketing authorization is NOT required because the device modification was specified in the PCCP, and it was implemented in conformance with PCCP. So, in this case, a new device modification would NOT require a new marketing submission.

MODIFICATION SCENARIO 2

Change: Does a Modification in input that was not specified in PCCP require a new marketing authorization?

Details:

Manufacture would like to deploy a modified ML model that uses images captured by thermographic camera

However, a new camera technology was not specified in PCCP

MODIFICATION SCENARIO 2- RESPONSE

Change: Does a Modification in input that was not specified in PCCP require a new marketing authorization?

Answer: YES a new marketing authorization is needed. Because this modification was NOT included in the PCCP, and it COULD significantly affect safety or effectiveness of the device, a new marketing submission would be required.

MODIFICATION SCENARIO 3

Change: Does a Modification related to the device's use and performance which was not specified in the PCCP require a new marketing authorization?

Details:

1) The manufacturer would like to distribute a new version of the ML-DSF that is patient-facing.
2) The ML-DSF would provide an analysis of physiological characteristics of skin lesions as it does not currently, and direct patients to follow-up with a dermatologist based on preliminary analysis of the malignancy of the skin lesion.
3) Modification introduces many new unconsidered risks, given that the modified ML-DSF will be patient-facing.

MODIFICATION SCENARIO 3 -RESPONSE

Change: Does a Modification related to the device's use and performance which was not specified in the PCCP require a new marketing authorization?

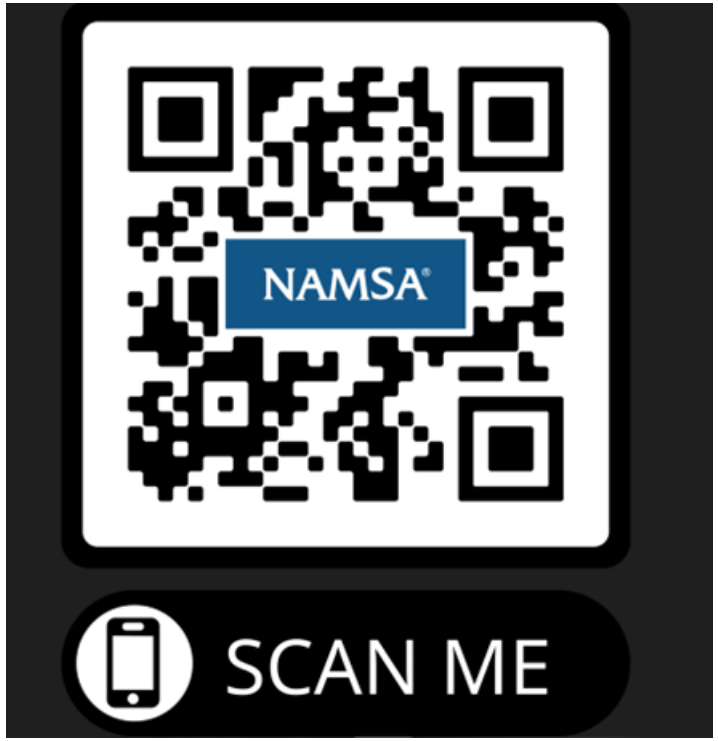
Answer: YES – a new marketing authorization is required because this modification was NOT included in the PCCP, and it could significantly affect safety or effectiveness of the device, a new marketing submission would be required.

CLARITY SURROUNDING ADAPTIVE LEARNING

1) The guidance is not clear whether or not adaptive learning is within scope of the regulatory framework.
2) The draft PCCP Guidance states in multiple locations the requirement for design verification and validation is needed for every change, which requires that a design change as part of design controls be applied before release of the change. The burden of following a design change process limits the use of the PCCP draft guidance to locked algorithms and not adaptive.
3) The guidance could improve by providing specific scenarios related to PMA's and IVD's.

CONCLUSION

- The PCCP draft guidance is a significant step forward in FDA's ability to effectively regulate AI/ML-enabled medical devices.
- It is the most rigorous treatment of regulating AI/ML-enabled medical devices globally.
- No other regulatory body/government authority has made the progress that the FDA has to date.
- Manufacturers are encouraged to carefully review the PCCP draft guidance and note the scope of PCCP (changes otherwise requiring submission).
- Manufactures should assess how the guidance supports adaptive learning and whether the need for design controls to modifications seem appropriate.



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