Predetermined Change Control Plans for Medical Devices

Draft Guidance for Industry and Food and Drug Administration Staff

DRAFT GUIDANCE

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Preface

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Draft Guidance for Industry and Food and Drug Administration Staff

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA or Agency) on this topic. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. To discuss an alternative approach, contact the FDA staff or Office responsible for this guidance as listed on the title page.

I. Introduction

On December 29, 2022, section 3308 of the Food and Drug Omnibus Reform Act of 2022, Title III of Division FF of the Consolidated Appropriations Act, 2023, Pub. L. No. 117-328 ("FDORA") added section 515C "Predetermined Change Control Plans for Devices" to the Federal Food, Drug, and Cosmetic (FD&C) Act. Section 515C of the FD&C Act (21 U.S.C. 360e-4) has provisions regarding predetermined change control plans (PCCPs) for devices requiring premarket approval (PMA) or premarket notification (510(k)). A PCCP is the documentation describing what modifications will be made to a device and how the modifications will be assessed. This draft guidance provides FDA's current thinking on a policy for PCCPs and recommendations on the information to include in a PCCP in a marketing submission for a device. This draft guidance recommends that a PCCP describe the planned device modifications, the associated methodology to develop, validate, and implement those modifications, and an assessment of the impact of those modifications. FDA reviews the PCCP as part of a marketing submission for a device to ensure the continued safety and effectiveness of the device without necessitating additional marketing submissions for implementing each modification described in the PCCP.

Upon finalization of this guidance, we will make conforming Level 2 updates to the following guidance documents to clarify that a PMA supplement or 510(k) is not required for a change to a device consistent with an approved or cleared PCCP[1]:

[1] Section 515C(a)(1) and 515C(b)(1) of the FD&C Act.

- "Modifications to Devices Subject to Premarket Approval (PMA) - The PMA Supplement Decision-Making Process"
- "Deciding When to Submit a 510(k) for a Change to an Existing Device"
- "Deciding When to Submit a 510(k) for a Software Change to an Existing Device"

Upon finalization of this guidance, we may also make Level 2 updates to the "Marketing Submission Recommendations for a Predetermined Change Control Plan for Artificial Intelligence/Machine Learning (AI/ML)-Enabled Device Software Functions" guidance document and other device-specific guidance documents containing information on PCCPs for consistency with this guidance.

This guidance has been prepared by the Center for Devices and Radiological Health (CDRH) and the Center for Biologics Evaluation and Research (CBER) in consultation with the Center for Drug Evaluation and Research (CDER) and the Office of Combination Products (OCP) in the Office of the Commissioner.

In general, FDA's guidance documents do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidances means that something is suggested or recommended, but not required.

II. Background

The concept of a PCCP is not entirely new to FDA. For example, in 2017, FDA described in the "Deciding When to Submit a 510(k) for a Change to an Existing Device" guidance that changes in the expiration date for use of a device generally do not require submission of a new 510(k) when the same methods or protocols that are described in the previously cleared 510(k) are used to support the change. In 2022, FDA described in the "Replacement Reagent and Instrument Family Policy for In Vitro Diagnostic Devices" guidance how manufacturers may add certain additional instruments for use with an in vitro diagnostic (IVD) assay that was previously cleared for use with a specific instrument without submission of a new 510(k), in part, by conducting a risk-based assessment and design verification and/or validation activities to assess the use of the IVD assay with the new instrument(s).

In 2019, FDA introduced the term and description of a PCCP in the "Proposed Regulatory Framework for Modifications to Artificial Intelligence/Machine Learning (AI/ML)-Based Software as a Medical Device (SaMD) - Discussion Paper and Request for Feedback."[2] This discussion paper described a potential approach to premarket review of PCCPs for AI/ML-based software modifications. On December 29, 2022, FDORA was enacted. Section 3308 of this legislation, titled "Predetermined Change Control Plans for Devices," amended the FD&C Act to add section 515C, which has provisions regarding PCCPs for devices that would otherwise

[2] Also available at FDA's website on "Artificial Intelligence and Machine Learning in Software as a Medical Device."

require a PMA supplement or a new 510(k). In 2023, we issued a draft guidance titled "Marketing Submission Recommendations for a Predetermined Change Control Plan for Artificial Intelligence/Machine Learning (AI/ML)-Enabled Device Software Functions," which incorporated stakeholder feedback on the discussion paper and reflected our initial thinking on the statutory change and the types of information we recommend be included in a PCCP in a marketing submission. In that draft guidance, we proposed a policy to support iterative improvement through prospective FDA review and authorization of modifications to an AI/ML-enabled device software function while continuing to provide a reasonable assurance of device safety and effectiveness. That draft guidance provided recommendations on the information to include in a PCCP in a marketing submission for an AI/ML-enabled device software function. We also proposed that a PCCP should include information on the following topics that could be divided into three categories: Description of Modifications (a detailed description of the specific, planned device modifications), Modification Protocol (the associated methodology to develop, validate, and implement those modifications), and Impact Assessment (the assessment of the benefits and risks of implementing a PCCP and the plan for risk mitigation).

In other device-specific guidance, FDA has also recommended using PCCPs to implement specific modifications for certain device types. For example, later in 2023, we issued a final guidance titled "Antimicrobial Susceptibility Test (AST) System Devices – Updating Breakpoints in Device Labeling" describing how manufacturers may use PCCPs to update susceptibility test interpretative criteria and associated performance in device labeling in response to changes posted on the FDA-Recognized Antimicrobial Susceptibility Test Interpretive Criteria website.

This broader draft guidance focuses on section 515C(a)-(c) of the FD&C Act, reproduced below, and provides FDA's policy and recommendations for marketing submissions for PCCPs for all device types.

SECTION 515C. [21 U.S.C. 360e–4] PREDETERMINED CHANGE CONTROL PLANS FOR DEVICES.

(a) APPROVED DEVICES.—

(1) IN GENERAL.—Notwithstanding section 515(d)(5)(A), a supplemental application shall not be required for a change to a device approved under section 515, if such change is consistent with a predetermined change control plan that is approved pursuant to paragraph (2).

(2) PREDETERMINED CHANGE CONTROL PLAN.—The Secretary may approve a predetermined change control plan submitted in an application, including a supplemental application, under section 515 that describes planned changes that may be made to the device (and that would otherwise require a supplemental application under section 515), if the device remains safe and effective without any change.

(3) SCOPE.—The Secretary may require that a change control plan include labeling required for safe and effective use of the device as such device changes pursuant to such plan, notification requirements if the device does not function as intended pursuant to such plan, and performance requirements for changes made under the plan.

(b) CLEARED DEVICES.—

(1) IN GENERAL.—Notwithstanding section 510(k), a premarket notification shall not be required for a change to a device cleared under section 510(k), if such change is consistent with an established predetermined change control plan granted pursuant to paragraph (2).

(2) PREDETERMINED CHANGE CONTROL PLAN.—The Secretary may clear a predetermined change control plan submitted in a notification submitted under section 510(k) that

describes planned changes that may be made to the device (and that would otherwise require a new notification), if—

(A) the device remains safe and effective without any such change; and

(B) the device would remain substantially equivalent to the predicate.

(3) SCOPE.—The Secretary may require that a change control plan include labeling required for safe and effective use of the device as such device changes pursuant to such plan, notification requirements if the device does not function as intended pursuant to such plan, and performance requirements for changes made under the plan.

(c) PREDICATE DEVICES.—In making a determination of substantial equivalence pursuant to section 513(i), the Secretary shall not compare a device to changed versions of a device implemented in accordance with an established predetermined change control plan as a predicate device. Only the version of the device cleared or approved, prior to changes made under the predetermined change control plan, may be used by a sponsor as a predicate device.

III. Scope

This draft guidance proposes recommendations on the types of modifications that, at this time, FDA believes generally may be appropriate for inclusion in a PCCP, and the information that should be included in a PCCP in a marketing submission[3] for any device type.

For purposes of this guidance, a PCCP includes those device modifications that generally would otherwise require a new marketing submission.[4,5] These modifications include those that could significantly affect,[6] or that otherwise affect,[7] the safety or effectiveness of the device,[8] unless those modifications are covered by an authorized PCCP. By including a PCCP in a marketing submission for a device, manufacturers can prospectively specify and seek premarket authorization[9] for intended modifications to a device without needing to submit additional marketing submissions or obtain further FDA authorization before implementing such modifications – provided the changes are implemented consistent with the PCCP that has been

[3] For purposes of this guidance, the term "marketing submission" includes a PMA application, 510(k) submission, or De Novo Classification request.

[4] For purposes of this guidance, unless otherwise stated, references to "device modifications" or "modifications" are those that generally would otherwise require a new marketing submission pursuant to 21 CFR 807.81(a)(3) and 21 CFR 814.39(a).

[5] For more information on whether a modification would require a new marketing submission, see the FDA guidances "Modifications to Devices Subject to Premarket Approval (PMA) – The PMA Supplement Decision-Making Process," "Deciding When to Submit a 510(k) for a Change to an Existing Device," or "Deciding When to Submit a 510(k) for a Software Change to an Existing Device," referred to as the "Device Modifications guidances" hereafter.

[6] 21 CFR 807.81(a)(3).

[7] 21 CFR 814.39(a).

[8] In accordance with 21 CFR 807.81(a)(3), a 510(k) is required for significant changes or modifications to a device and include 1) those that "could significantly affect the safety or effectiveness of the device, e.g., a significant change or modification in design, material, chemical composition, energy source, or manufacturing process" or include 2) "a major change or modification in the intended use of the device." In accordance with 21 CFR 814.39(a), a PMA supplement is required for "change[s] affecting the safety or effectiveness of the device" unless an exception applies (see 21 CFR 814.39). For simplicity, in this guidance, the phrase "significant changes" or "significant modifications" refers to 21 CFR 807.81(a)(3). However, for devices subject to PMA requirements, the broader requirement pursuant to 21 CFR 814.39(a) of a "change affecting the safety or effectiveness" applies.

[9] For purposes of this guidance, the term "authorization" includes approval of a PMA application, clearance of a 510(k) submission, or grant of a De Novo Classification request.

reviewed and established through a device marketing authorization (referred to hereafter as the "authorized PCCP").[10] In other words, obtaining FDA authorization of a PCCP as part of a marketing submission for a device allows a manufacturer to modify its device over time in accordance with the PCCP instead of obtaining separate FDA authorization for each significant change prior to each implementation.[11]

Because a PCCP is appropriate for device modifications that generally would otherwise require a new marketing submission,[12] this guidance does not address a plan that only contains a proposal for modifications that would not require a new marketing submission. For such modifications, the Quality System regulation (QSR) (21 CFR Part 820)[13] requires manufacturers of finished medical devices to, among other things, document the change in the device master record.[14] For devices subject to PMA requirements, such modifications need to be reported to FDA in post-approval periodic reports required as a condition to approval of the device.[15]

Premarket authorization for a device with a PCCP may be established through the PMA pathway (see section 515C(a) of the FD&C Act), the 510(k) pathway (see section 515C(b) of the FD&C Act), or the De Novo pathway (see section 513(f)(2) of the FD&C Act).[16] For devices subject to 510(k) requirements, 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.[17]

[10] For purposes of this guidance, the term "authorized PCCP" refers to a PCCP that has been reviewed and established through a device marketing authorization.

[11] Sections 515C(a)(1) and 515C(b)(1) of the FD&C Act, 21 CFR 807.81(a)(3), and 21 CFR 814.39(a).

[12] 21 CFR 807.81(a)(3) and 21 CFR 814.39(a).

[13] On February 2, 2024, FDA issued a final rule amending the device QSR, 21 CFR Part 820, to align more closely with international consensus standards for devices (89 FR 7496). This final rule will take effect on February 2, 2026. Once in effect, this rule will withdraw the majority of the current requirements in Part 820 and instead incorporate by reference the 2016 edition of the International Organization for Standardization (ISO) 13485, Medical devices – Quality management systems – Requirements for regulatory purposes, in Part 820. As stated in the final rule, the requirements in ISO 13485 are, when taken in totality, substantially similar to the requirements of the current Part 820, providing a similar level of assurance in a firm's quality management system and ability to consistently manufacture devices that are safe and effective and otherwise in compliance with the FD&C Act. When the final rule takes effect, FDA will also update the references to provisions in 21 CFR Part 820 in this guidance to be consistent with that rule.

[14] 21 CFR 820.181.

[15] See 21 CFR 814.39(b) and 21 CFR 814.82(a)(7) and FDA's guidance "Annual Reports for Approved Premarket Approval Applications (PMA)."

[16] The De Novo classification process allows FDA to classify a device into class I or II when general controls or general controls and special controls provide a reasonable assurance of safety and effectiveness, but for which there is no legally marketed predicate. The De Novo pathway, therefore, allows FDA to develop special controls that provide a reasonable assurance of the safety and effectiveness of the subject device. At this time, FDA expects that if it authorizes a device with a PCCP via the De Novo pathway, the Agency would develop appropriate special controls, which may include specific requirements for a PCCP.

[17] See section 515C(c) of the FD&C Act.

Generally, the recommendations in this guidance apply to the device constituent part[18] of device-led[19] combination products.[20] The recommendations in this guidance do not apply to the drug or biologic constituent part of device-led combination products. For device-led combination products with a PCCP, the FDA review division will consult CBER or CDER, as appropriate.

FDA highly encourages early engagement regarding a proposed PCCP with the FDA review division; in particular, early engagement could be especially helpful for certain devices, including combination products and high-risk, life-sustaining, life-supporting, or implantable devices. FDA encourages manufacturers to leverage the Q-Submission Program[21] for obtaining FDA feedback on a proposed PCCP for a device prior to submitting a marketing submission. The FDA review division with purview over the device will provide feedback on a proposed PCCP, including whether the scope of the modifications is appropriate for inclusion in a PCCP and, based on the statutory and regulatory requirements applicable to that device, what evidence and information would ensure that the device under that PCCP remains safe and effective under section 515C of the FD&C Act.

This draft guidance is intended to provide recommendations on the information to include in a PCCP in a marketing submission for a device. This draft guidance is not intended to provide a complete description of what may be necessary to include in a marketing submission for a device.[22] The proposed recommendations in this draft guidance do not change applicable statutory and regulatory standards, such as device clearance or approval standards, nor the applicable requirements, including marketing submission content requirements and the requirements for valid scientific evidence.[23] FDA recommends that you refer to other guidances, as applicable to a specific device, for recommendations on aspects of the submission beyond the PCCP.

This draft guidance is intended to provide recommendations on the types of modifications that, at this time, FDA believes generally may be appropriate for inclusion in a PCCP for a device. This draft guidance is not intended to delineate a comprehensive list of modifications FDA would consider appropriate for inclusion in a PCCP for a device. However, the draft guidance proposes types of modifications that generally may be appropriate (see Section VI. of this guidance) and provides illustrative examples (see Section VIII. of this guidance).

IV. Guiding Principles for PCCPs

In developing this guidance for manufacturers and FDA staff on PCCPs for all device types, several guiding principles were followed. Some derive from existing policies and others are key to understanding the policy proposed in this draft guidance. Anyone using this draft guidance

[18] See 21 CFR 4.2.
[19] See 21 CFR 3.4 for information on lead center assignment.
[20] See 21 CFR 3.2(e).
[21] See FDA's guidance "Requests for Feedback and Meetings for Medical Device Submissions: The Q-Submission Program," hereafter referred to as the "Q-Submission Program."
[22] See, e.g., 21 CFR 807.87, 21 CFR 860.220, or 21 CFR 814.20.
[23] See, e.g., 21 CFR 807.87, 21 CFR 860.220, or 21 CFR 814.20, and 21 CFR 860.7(c).

should bear in mind the following guiding principles:

- **Reasonable assurance of safety and effectiveness and substantial equivalence of devices with PCCPs** – A PCCP is part of the device marketing authorization. As such, for the PCCP to be authorized with the device, the totality of the information included in a PCCP should enable FDA to assess the reasonable assurance of safety and effectiveness or substantial equivalence of the device.[24]

- **PCCPs may be a least burdensome option to support device modifications** – Manufacturers may wish to use PCCPs as a way to implement modifications to their devices without needing to submit a new marketing submission for each modification while continuing to provide a reasonable assurance of device safety and effectiveness. When used appropriately, PCCPs are expected to be least burdensome[25] for manufacturers and FDA. However, PCCPs are optional. FDA will review the device and PCCP and determine the acceptability of a proposed PCCP in accordance with applicable device approval or clearance standards under the FD&C Act and its implementing regulations.[26] FDA's review of the device and PCCP will follow a risk-based approach with consideration of the device's intended use and technological characteristics, as well as the regulatory history of the specific device, device type, and manufacturer, and use FDA's benefit-risk framework.[27]

- **PCCPs are part of a device's marketing authorization** – A PCCP is part of the device's marketing authorization, and as such, the manufacturer is required to implement modifications consistent with their authorized PCCP, when the manufacturer chooses to implement those modifications and use the PCCP to do so.[28] Premarket authorization of a PCCP is based on the details of the specific PCCP developed by the manufacturer for that specific device. When a manufacturer includes a PCCP in a marketing submission for a device, the FDA review division with purview over the device will determine the acceptability of a proposed PCCP. This will include whether the scope of the modifications is appropriate for inclusion in a PCCP and, based on the statutory and regulatory requirements applicable to that device, what information and evidence would ensure that the device under that PCCP remains safe and effective under section 515C of the FD&C Act. When the PCCP is authorized, the PCCP is a part of the marketing authorization of a device and will be included in the device's letter of authorization.

- **PCCPs are specific** – A PCCP should include specific modifications that the manufacturer intends to make over time that generally would otherwise require a new

[24] See, e.g., sections 513(i)(1) and 515C of the FD&C Act and 21 CFR 860.7.
[25] See FDA's guidance "The Least Burdensome Provisions: Concept and Principles."
[26] Sections 513(a)(3)(D)(iv), 513(i)(1)(D)(iii), and 515(c)(5)(D) of the FD&C Act.
[27] See FDA's guidances "Factors to Consider When Making Benefit-Risk Determinations in Medical Device Premarket Approval and De Novo Classifications" and "Benefit-Risk Factors to Consider When Determining Substantial Equivalence in Premarket Notifications (510(k)) with Different Technological Characteristics."
[28] See sections 515C(a)(1) and 515C(b)(1) of the FD&C Act.

marketing submission.[29] A PCCP should not include a list of any/all modifications that a manufacturer may possibly make. To ensure a timely and efficient review, a PCCP should include only a few, specific modifications that can be verified and validated. The modifications included in a PCCP must maintain the device within the device's intended use,[30] and as applicable, must allow the device to remain substantially equivalent to the predicate device.[31] If a PCCP includes numerous modifications, or modifications that range across various aspects of the device, FDA may not be able to make a determination of reasonable assurance of safety and effectiveness or substantial equivalence for the device and its PCCP.

- **PCCPs harmonize with existing FDA Device Modifications guidances** – Manufacturers can use a PCCP as a way to implement modifications to their devices without needing to submit a new marketing submission for each modification. The Device Modifications guidances help manufacturers determine whether a new marketing submission is required for a modification to their device,[32] for example, when the device does not have a PCCP, or when the modification is not consistent with the PCCP. FDA believes this guidance and the Device Modifications guidances support improvement through modifications to devices while continuing to provide a reasonable assurance of device safety and effectiveness.

V. Policy for PCCPs

An authorized PCCP specifies planned modifications that, if not included in a PCCP, could otherwise require a new marketing submission pursuant to 21 CFR 807.81(a)(3) and 21 CFR 814.39(a), and consistent with the Device Modifications guidances. Because modifications that are specified and implemented in accordance with an authorized PCCP were reviewed and authorized through the marketing submission containing the PCCP, the modifications can be implemented to the device without triggering the need for a new marketing submission.[33]

FDA would consider it to be a deviation from the authorized PCCP in circumstances where the PCCP is not followed or cannot be followed.[34] Deviations from the authorized PCCP could significantly affect the safety or effectiveness of the device. This could include, for example, issues related to the Modification Protocol, such as failure to meet pre-specified performance criteria. Device modifications that would not require a marketing submission would not be considered a deviation from an authorized PCCP.[35] However, significant modifications made to

[29] 21 CFR 807.81(a)(3) and 21 CFR 814.39(a).
[30] See sections 515C(a)(2) and 515C(b)(2) of the FD&C Act.
[31] Section 515C(b)(2)(B) of the FD&C Act.
[32] 21 CFR 807.81(a)(3) and 21 CFR 814.39(a).
[33] Sections 515C(a)(1) and 515C(b)(1) of the FD&C Act, 21 CFR 807.81(a)(3), and 21 CFR 814.39(a).
[34] FDA would not consider it to be a deviation from the authorized PCCP in situations where a manufacturer chooses not to implement modifications in their authorized PCCP or where a manufacturer chooses to submit a new marketing submission for a device modification in lieu of using their authorized PCCP.
[35] See Section V.D. of this guidance for further details on implementing device modifications that may or may not require a new marketing submission in accordance with 21 CFR 807.81(a)(3) and 21 CFR 814.39(a).

a device that are not specified in, or implemented in accordance with, the authorized PCCP likely require a new marketing submission prior to implementation of the modification.[36] Deviations from the authorized PCCP reviewed in the marketing submission would generally cause the device to be adulterated and misbranded under sections 501(f)(1) and 502(o) of the FD&C Act, respectively. The introduction or delivery for introduction into interstate commerce of any food, drug, device, tobacco product, or cosmetic that is adulterated or misbranded is prohibited under section 301(a) of the FD&C Act, and where appropriate, FDA may take legal or regulatory action against violations of prohibited acts, including, without limitation, seizure or injunction.

A. Components of a PCCP

A PCCP should consist of a detailed Description of Modifications, a Modification Protocol, and an Impact Assessment (see Section VII. of this guidance) because these components are intended to provide FDA with information that will enable our review of the proposed modifications. The detailed Description of Modifications should outline the specific, planned modifications that may be made to the device. This includes defining the specifications for the characteristics and performance of the planned modifications to the device. The Modification Protocol should describe the verification and validation activities, including pre-defined acceptance criteria, that will support each modification to assure the device remains safe and effective across the intended use populations. The Impact Assessment helps to tie the Description of Modifications to the Modification Protocol in that the Impact Assessment identifies the benefits and risks introduced by the specified, planned modifications and addresses how the verification and validation activities of the Modification Protocol will continue to assure the safety and effectiveness of the device. The detailed Description of Modifications, Modification Protocol, and Impact Assessment are all interrelated components of a PCCP.

B. Establishing a PCCP

Premarket authorization for a device with a PCCP must be established through the PMA pathway, 510(k) pathway, or De Novo pathway, as appropriate, as a PCCP must be reviewed and established as part of a marketing authorization[37,38] for a device prior to a manufacturer implementing any modifications under that PCCP. In general, FDA considers the following submission types to be appropriate[39] to establish a PCCP:

- For devices subject to PMA requirements:
    - Original PMA application
    - Modular PMA application, where a PCCP comprises a module of review
    - 180-Day PMA supplement

[36] 21 CFR 807.81(a)(3) and 21 CFR 814.39(a).
[37] See sections 513(f)(2) and 515C of the FD&C Act.
[38] This includes marketing authorization for a device and PCCP where the device or a derivative thereof has yet to be introduced into interstate commerce, or marketing authorization for a device or a derivative thereof has been introduced into interstate commerce, and for which is being modified to add a PCCP.
[39] Submission types for which FDA does not make an affirmative decision (i.e., authorization) would not be appropriate to establish a PCCP.

405 - 135-Day PMA supplement, where a PCCP comprises certain manufacturing
406 changes only
407 - Panel Track PMA supplement
408 - Real-Time PMA supplement, where a PCCP comprises minor changes and the
409 manufacturer and FDA agree that the review can be achieved in a real-time
410 setting[40,41]
411 • For devices subject to 510(k) requirements:
412 - Traditional 510(k) submission
413 - Abbreviated 510(k) submission[42]
414 • For devices subject to De Novo requirements:
415 - Original De Novo request
416
417 A PCCP is authorized as part of the device marketing authorization. FDA must reach a
418 determination[43] of reasonable assurance of safety and effectiveness or substantial equivalence in
419 review of the device, including each modification specified in the PCCP, for the PCCP to be
420 authorized with the device.
421
422 As manufacturers implement modifications included in an authorized PCCP, FDA expects
423 manufacturers to implement the modifications consistent with their authorized PCCP, i.e., in
424 accordance with their Modification Protocol. A manufacturer must implement any changes in
425 accordance with their quality system.[44] A manufacturer's quality system is critical for change
426 management processes for a device, especially for devices that include a PCCP, because a PCCP
427 includes modifications that generally would otherwise require a new marketing submission.[45]
428 Compliance with the QSR is essential in order for a manufacturer to implement modifications
429 consistent with their authorized PCCP and failure to do so could potentially present a serious risk
430 to human health.
431
432 Under section 515C(a)(2) of the FD&C Act, FDA may approve a PCCP submitted in a PMA.
433 Under section 515(d)(2)(C) of the FD&C Act, FDA must deny approval of a PMA if FDA finds
434 that the methods used in, or the facilities or controls used for, the manufacture, processing,
435 packing, or installation of such device do not conform to the QSR requirements. Thus, consistent
436 with sections 515C(a)(2) and 515(d)(2)(C) of the FD&C Act, FDA must deny approval of a
437 PCCP submitted in a PMA if FDA finds that the methods used in, or the facilities or controls
438 used for, the manufacture, processing, packing, or installation of the subject device do not
439 conform to the QSR requirements.
440

[40] Section 737(4)(D) of the FD&C Act defines a real-time supplement as "a supplement to an approved premarket application or premarket report under section 515 that requests a minor change to the device, such as a minor change to the design of the device, software, sterilization, or labeling, and for which the applicant has requested and the agency has granted a meeting or similar forum to jointly review and determine the status of the supplement."
[41] See FDA's guidance "Real-Time Premarket Approval Application (PMA) Supplements."
[42] See FDA's guidance "The Abbreviated 510(k) Program."
[43] See, e.g., sections 513(i)(1) and 515C of the FD&C Act and 21 CFR 860.7.
[44] 21 CFR Part 820.
[45] Sections 515C(a)(2) and 515C(b)(2) of the FD&C Act, 21 CFR 807.81(a)(3), and 21 CFR 814.39(a).

Under section 515C(b)(2) of the FD&C Act, FDA may clear a PCCP submitted in a 510(k). Generally, under section 513(f)(5) of the FD&C Act, FDA may not withhold a determination of the initial classification of a device under section 513(f)(1) of the FD&C Act because of, among other things, a finding that the facility in which the device is manufactured is not in compliance with the QSR. However, also under section 513(f)(5), for devices subject to 510(k), FDA may withhold a substantial equivalence determination if FDA finds that there is a substantial likelihood that the failure to comply with QSR will potentially present a serious risk to human health. Thus, consistent with sections 515C(b)(2) and 513(f)(5) of the FD&C Act, FDA may under certain case-by-case circumstances withhold clearance of a PCCP submitted in a 510(k) based on findings in the regulatory history of the manufacturer that demonstrate failure to comply with QSR.

For devices subject to 510(k) requirements, the determination of substantial equivalence includes, among other requirements, a comparison between the technological characteristics of the predicate device and the subject device.[46] In FDA's determination of substantial equivalence, FDA considers the PCCP to be part of the technological characteristics of the device. For 510(k) submissions, 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.[47] Once a 510(k) for a device that includes modifications that have been implemented consistent with the authorized PCCP has been cleared in a subsequent marketing submission, such device can now serve as an eligible predicate device. The PCCP can be considered during the 510(k) review process at multiple points in the decision tree to address the critical questions in the 510(k) Decision-Making Flowchart.[48] In general, FDA anticipates that the PCCP will primarily be reviewed after FDA finds that the intended use of the subject device and the predicate device are the same, to help determine whether the devices have different technological characteristics that do not raise different questions of safety and effectiveness.[49]

FDA encourages manufacturers to leverage the Q-Submission Program to obtain FDA feedback on a proposed PCCP for a device and submission type prior to submitting a marketing submission. While manufacturers are encouraged to discuss their plans through a Pre-Submission, FDA does not authorize a PCCP in a Pre-Submission.

C. Identifying a PCCP in a Marketing Submission

The PCCP should be included as a standalone section within the marketing submission, with a title and version number. Additionally, it should be prominently included and discussed in the cover letter and included in the marketing submission's table of contents as "Predetermined Change Control Plan." The PCCP should be discussed in the marketing submission as part of the device description, labeling, and relevant sections used for the assessment of reasonable

[46] See section 513(i) of the FD&C Act.
[47] See section 515C(c) of the FD&C Act.
[48] See FDA's guidance "The 510(k) Program: Evaluating Substantial Equivalence in Premarket Notifications [510(k)]" Appendix A, Decision Points 1 through 4.
[49] See id. at Decision Points 5a and 5b.

assurance of safety and effectiveness or the substantial equivalence comparison. Any information pertaining to the PCCP content included outside of the PCCP section should include appropriate references to the PCCP section.

Device labeling must comply with applicable statutes and regulations.[50] FDA may require that a device with an authorized PCCP include labeling required for safe and effective use of the device as such device changes pursuant to such plan,[51] excluding, as appropriate, trade secret and confidential commercial information. In certain circumstances, for example, when an authorized PCCP is limited to manufacturing changes for a device, it may not be necessary to include information on a device's authorized PCCP in the labeling. However, in the majority of circumstances, information on the device and its authorized PCCP in the labeling is important in order for a user to use the device safely and effectively for the purposes for which it is intended. In particular, information on the device's authorized PCCP may be necessary for a user to understand changes in the device and to continue to use the device safely and effectively across the intended use populations and intended environments as the device changes pursuant to the authorized PCCP.

As stated above, in the majority of circumstances, FDA recommends that the labeling include a statement that the device has an authorized PCCP. When appropriate, including as modifications are implemented consistent with an authorized PCCP, FDA recommends that the labeling related to the PCCP be updated to include the relevant information listed below for the device and the PCCP so that users may be aware of modifications that have been implemented that impact use of the device:

- A description of the implemented modifications, including a summary of current device performance, associated inputs/outputs, validation requirements, and related evidence;
- A description of how the modifications were implemented; and
- A description of how users will be informed of implemented modifications, including, for example, updated instructions for use or a version history.

When utilizing an authorized PCCP to implement device modifications, the manufacturer should update the labeling for the device as specified in the authorized PCCP.[52]

[50] 21 CFR Part 801 (Labeling) and 21 CFR Part 809 (In Vitro Diagnostic Products for Human Use). See, e.g., 21 CFR 801.5 (requiring that labeling include adequate directions for use); 21 CFR 801.109(c) (for prescription devices, requiring that labeling include any relevant hazards, contraindications, side effects, and precautions under which practitioners licensed by law to administer the device can use the device safely and for the purpose for which it is intended); and 21 CFR 809.10(b)(6) (for in vitro diagnostic products, requiring labeling accompanying any instruments use or function, installation procedures, performance characteristics and specifications, service and maintenance information, etc.).

[51] See sections 515C(a)(3), 515C(b)(3), and 513(f)(2) of the FD&C Act.

[52] See Section VII.B.(2)b. for recommendations on update procedures in a Modification Protocol, which should address how labeling will be updated when modifications are implemented, as appropriate.

The PCCP should be described in publicly available device summaries, including, for example, the PMA summary of safety and effectiveness document (SSED) and approval order,[53] 510(k) summary,[54,55] or De Novo decision summary.[56] Details of the PCCP should be included in sufficient detail in the public-facing documents to support transparency to users of the assessment of reasonable assurance of safety and effectiveness or the substantial equivalence comparison for the device and the device's specifications, excluding, as appropriate, trade secret and confidential commercial information. In addition, FDA recommends public-facing documents include a summary of the following information regarding the PCCP, as appropriate:

- 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.

D. Utilizing an Authorized PCCP to Implement Device Modifications

FDA expects manufacturers to follow their authorized PCCP, and manufacturers are required to follow applicable legal requirements regarding the device and its authorized PCCP. In general, a PCCP should be evaluated within the existing risk management framework of the device and must be implemented in accordance with the manufacturer's quality system.[57]

Figure 1 depicts the process for implementing a modification to a device with an authorized PCCP. Manufacturers should first consider whether the particular modification is or is not consistent with the authorized PCCP; FDA considers a modification to be consistent with the

[53] In accordance with 21 CFR 814.9(e), "FDA will make available to the public … a detailed summary of information submitted to FDA respecting the safety and effectiveness of the device that is the subject of the PMA and that is the basis for the order."

[54] In accordance with 21 CFR 807.92, "a 510(k) summary shall be in sufficient detail to provide an understanding of the basis for a determination of substantial equivalence." This includes, but is not limited to, a description of the device, and for those 510(k) submissions in which a determination of substantial equivalence is also based on an assessment of performance data, non-clinical tests, and clinical tests.

[55] If a sponsor chooses to submit a 510(k) Statement rather than a 510(k) Summary, the sponsor should provide to requestors all PCCP information in the 510(k) that supports transparency to users of FDA's determination of substantial equivalence for the device and its specifications, as such information constitutes safety and effectiveness information. See 21 CFR 807.93 for requirements on the content and format of a 510(k) Statement.

[56] The De Novo decision summary is intended to present an objective and balanced summary of the scientific evidence that served as the basis for the FDA's decision to grant a De Novo request; see FDA's website on De Novo Classification Request.

[57] Manufacturers are required to comply with the QSR (21 CFR Part 820). The device and PCCP must be implemented consistent with 21 CFR Part 820, including, but not limited to design controls (21 CFR 820.30), nonconforming products (21 CFR 820.90), and corrective and preventative action (21 CFR 820.100). The QSR also includes requirements to review and approve modifications to device design and production (21 CFR 820.30 and 820.70), and requirements to document changes and approvals in the device master record (21 CFR 820.181).

authorized PCCP when the modification has been specified in the Description of Modifications included in the PCCP *and* has been implemented in accordance with the Modification Protocol. If the particular modification is consistent with the authorized PCCP, a new marketing submission is not necessary; the modification can be implemented in accordance with the Modification Protocol, and the manufacturer should document that modification and the analysis in accordance with the manufacturer's quality system.

If the particular modification is not consistent with the authorized PCCP – including if the modification is not included in the authorized PCCP or if the modification is included in the authorized PCCP but is not implemented in accordance with the methods and specifications described in the Modification Protocol – the manufacturer should then proceed to evaluate the particular modification as described below. As part of the review of the particular modification, manufacturers should consider how implementation of the particular modification may affect the PCCP for the device by reviewing the Impact Assessment of the PCCP to determine if the particular modification introduces or significantly modifies risk mitigations for the PCCP.

- If the modification is not included in the authorized PCCP, the manufacturer should proceed based on their evaluation of the particular modification in accordance with applicable FDA statutory and regulatory requirements and after consulting the Device Modifications guidances.
- If the modification is included in the authorized PCCP but is not implemented in accordance with the methods and specifications described in the Modification Protocol, in most cases, because modifications included in a PCCP are those that would generally otherwise require a new marketing submission, it is likely that a new marketing submission will be required before the manufacturer can implement the change.[58]

As described in the introduction of Section V. of this guidance, FDA would consider it to be a deviation from the authorized PCCP in circumstances where the PCCP is not followed or cannot be followed.[59] Deviations from the authorized PCCP could significantly affect the safety or effectiveness of the device. Significant modifications made to a device that are not specified in, or implemented in accordance with, the authorized PCCP likely require a new marketing submission.[60] If a manufacturer believes that the deviation from their authorized PCCP is not significant, we strongly encourage discussion with the appropriate FDA review division. In general, manufacturers may contact the appropriate FDA review division for a discussion about a proposed modification and whether it may be considered consistent with the authorized PCCP.

If, after review of applicable FDA statutory and regulatory requirements a new marketing submission is required,[61] the appropriate marketing submission could request authorization for:

[58] 21 CFR 807.81(a)(3) and 21 CFR 814.39(a).
[59] FDA would not consider it to be a deviation from the authorized PCCP in situations where a manufacturer chooses not to implement modifications in their authorized PCCP or where a manufacturer chooses to submit a new marketing submission for a device modification in lieu of using their authorized PCCP.
[60] 21 CFR 807.81(a)(3) and 21 CFR 814.39(a).
[61] 21 CFR 807.81(a)(3) and 21 CFR 814.39(a).

- A modification to the authorized PCCP[62] (see Section V.E. of this guidance); and/or
- The modified device (i.e., a device modification not implemented through a PCCP).

In each of these cases, the marketing submission for the modification must include the appropriate marketing submission requirements[63] for the device. If the manufacturer requests authorization for a modification to the authorized PCCP, the manufacturer must also submit the proposed, modified PCCP for the device.[64] If the manufacturer requests authorization for the modified device, the manufacturer must also submit the proposed PCCP for the modified device.[65] In both scenarios, the manufacturer must obtain FDA authorization for the device and proposed PCCP before implementing the PCCP.[66]

[62] A change to the authorized PCCP could include a change in Description of Modifications, the Modification Protocol, and/or the Impact Assessment, as appropriate.
[63] See, e.g., 21 CFR 807.87, 21 CFR 860.220, or 21 CFR 814.20. In general, manufacturers may provide references in the marketing submission to prior marketing submissions for content that remains unchanged, as appropriate.
[64] Sections 515C(a)(2) and 515C(b)(2) of the FD&C Act.
[65] Sections 515C(a)(2) and 515C(b)(2) of the FD&C Act.
[66] Section 515C of the FD&C Act, 21 CFR 807.81(a)(3), and 21 CFR 814.39(a).

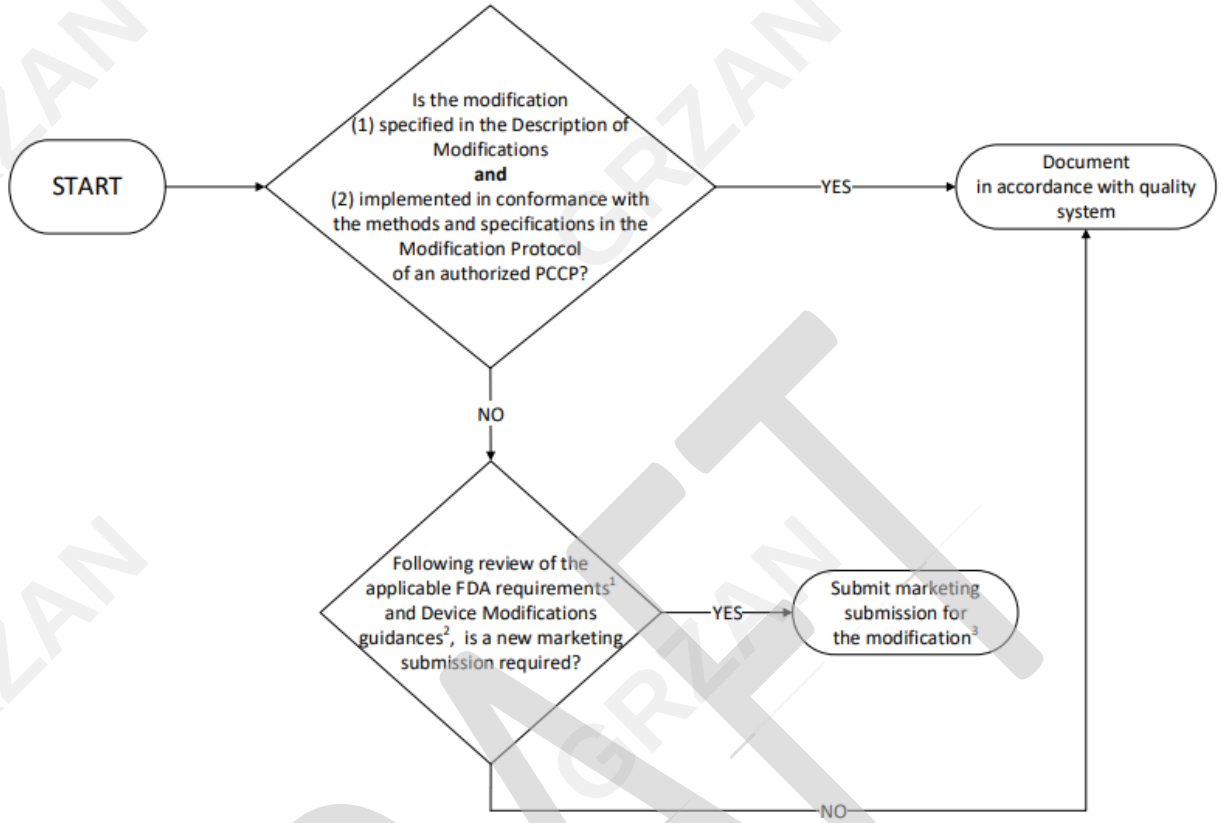


Figure 1. Implementing a Modification to a Device with an Authorized PCCP

E. Modifying a Previously Authorized PCCP

FDA believes that modifications to an authorized PCCP will generally constitute changes to the device that would otherwise require a new marketing submission.[67] In other words, FDA anticipates that modifications to a PCCP will need to be reviewed and established as part of the marketing submission for the modified device because a modification to the PCCP will generally significantly affect the safety or effectiveness of the device.[68]

[67] Sections 515C(a)(2) and 515C(b)(2) of the FD&C Act, 21 CFR 807.81(a)(3), and 21 CFR 814.39(a).
[68] Sections 515C(a)(2) and 515C(b)(2) of the FD&C Act, 21 CFR 807.81(a)(3), and 21 CFR 814.39(a).

For a manufacturer who would like to modify their PCCP for a previously authorized device with a PCCP,[69] the marketing submission must include the appropriate marketing submission requirements[70] and the proposed, modified PCCP for the device.[71] We recommend that manufacturers provide a summary of the changes to the authorized PCCP, and where practicable, a tracked changes version compared to the authorized PCCP. In general, FDA considers the PMA supplement and 510(k) submission types included in Section V.B. of this guidance to be appropriate to modify a PCCP. In addition to those submission types, for devices subject to 510(k) requirements, a special 510(k) submission may be appropriate to modify a PCCP where the modifications to a PCCP comprise changes to the manufacturer's own device and PCCP and where well-established methods are available to evaluate the change to the PCCP.[72]

FDA intends to focus its review on the aspects of the device that are most significantly modified.[73] For example, if the device has been relatively unchanged since FDA's prior authorization and a modified PCCP is proposed, FDA would focus its review on the modified PCCP. Manufacturers may discuss proposed changes to the PCCP with the appropriate FDA review division through the Q-Submission Program.

F. Version Control and Maintenance of a PCCP for a Device

At this time, as manufacturers gain experience developing and implementing PCCPs, FDA anticipates that review of a marketing submission that includes a PCCP will be interactive. It is possible that a PCCP submitted as part of a marketing submission may need revisions before FDA can make a determination[74] of reasonable assurance of safety and effectiveness or substantial equivalence in review of the device, including each modification in the PCCP, for the PCCP to be authorized with the device. FDA should work with the manufacturer to revise the PCCP, and will do so using FDA's existing processes to request additional information through interactive review or through a deficiency letter.[75] If deficiencies with the PCCP remain unresolved, FDA may authorize the device upon withdrawal of the PCCP.

As described in Section V.C. of this guidance, a copy of the PCCP with a title and version number should be included in the marketing submission for the device. If the PCCP is revised during review, such as in response to deficiencies, a final, revised version of the PCCP should be submitted as a clean copy to FDA and should include a title and current version number for the PCCP. FDA authorizes the PCCP as part of the marketing authorization of a device. To that end,

[69] E.g., through a PMA supplement or a traditional 510(k) for a device that has already been authorized.
[70] See, e.g., 21 CFR 807.87, 21 CFR 860.220, or 21 CFR 814.20. In cases where the modified PCCP is the reason for the marketing submission, and in general, manufacturers may provide references in the marketing submission to prior marketing submissions for content that remains unchanged, as appropriate.
[71] Sections 515C(a)(2) and 515C(b)(2) of the FD&C Act.
[72] See FDA's guidance "The Special 510(k) Program."
[73] Note that "focus of the review" is not intended to imply a review of the PCCP *only*; rather, the focus on the PCCP is as a significant change to the device that could affect the safety or effectiveness of the device.
[74] See, e.g., sections 513(i)(1) and 515C of the FD&C Act and 21 CFR 860.7.
[75] See FDA's guidance, "Developing and Responding to Deficiencies in Accordance with the Least Burdensome Provisions."

the PCCP will be referenced in the device's letter of authorization, including the PCCP title and version number. A manufacturer should only have one version of an authorized PCCP for their device. However, a PCCP can evolve over time through future marketing submissions where a new version of the PCCP can be authorized. As such, there should only be one version of the PCCP under review with a device at any given time to help with version control of the PCCP for manufacturers and FDA.

Over time, as a manufacturer implements their authorized PCCP for their device, they may wish to make modifications to the device that are not included in their authorized PCCP and that may require a new marketing submission.[76] If prior modifications have been implemented consistent with the authorized PCCP for the device, the new marketing submission for the device should include a summary of those modifications that have been implemented. This may include information in the device description, labeling, and other relevant sections of the marketing submission so that FDA can understand the current device characteristics and performance. In the context of premarket authorization, FDA does not intend to re-review the adequacy of modifications implemented consistent with an authorized PCCP; however, FDA needs to have an understanding of the current device characteristics and performance in order to make a determination[77] of reasonable assurance of safety and effectiveness or substantial equivalence. Additionally, if the manufacturer would also like to modify their previously authorized PCCP, the marketing submission must include the appropriate marketing submission requirements[78] and the proposed, modified PCCP for the device (see Section V.E. of this guidance).[79]

For devices subject to PMA requirements, submission of periodic reports, at intervals of one year (unless otherwise specified) from the date of approval of the original PMA are required under 21 CFR 814.84. The Annual Report must include, separately for each model number (if applicable), the number of devices sold and distributed during the reporting period, including those distributed to distributors.[80] FDA recommends that the Annual Report include a separate section that describes any changes implemented through an approved PCCP. Additionally, for devices subject to PMA requirements, when a modification implemented consistent with the authorized PCCP necessitates an update to the labeling, manufacturers should provide a summary of the updated labeling in the annual report.[81]

For devices subject to 510(k) requirements, a manufacturer must compare their subject device to the version of the predicate device cleared or approved prior to changes made under the PCCP.[82] However, once a 510(k) for a device that includes modifications that have been implemented

[76] 21 CFR 807.81(a)(3) and 21 CFR 814.39(a).
[77] See, e.g., sections 513(i)(1) and 515C of the FD&C Act and 21 CFR 860.7.
[78] See, e.g., 21 CFR 807.87, 21 CFR 860.220, or 21 CFR 814.20. In general, manufacturers may provide references in the marketing submission to prior marketing submissions for content that remains unchanged, as appropriate.
[79] Sections 515C(a)(2) and 515C(b)(2) of the FD&C Act.
[80] See 21 CFR 814.82(a)(9) (noting that "[s]uch other requirements as FDA determined are necessary to provide reasonable assurance, or continued reasonable assurance, of the safety and effectiveness of the device" may be included as post-approval requirements for a PMA-approved device).
[81] See FDA's guidance "Annual Reports for Approved Premarket Approval Applications (PMA)."
[82] Section 515C(c) of the FD&C Act.

consistent with the authorized PCCP has been cleared in a subsequent marketing submission, such device can now serve as an eligible predicate device.

VI. Types of Modifications

Modifications that are appropriate for inclusion in a PCCP include those that are intended to maintain or improve the safety or effectiveness of the device. Modifications should also be specific, and should be able to be verified and validated.

Modifications included in a PCCP must maintain the device within the device's intended use,[83] and as applicable, must allow the device to remain substantially equivalent to the predicate device.[84] In general, FDA believes that modifications included in a PCCP should also maintain the device within the device's indications for use.[85] As with modifications to the intended use, FDA believes that most modifications to the indications for use included in a PCCP would be difficult for FDA to assess prospectively to determine whether the device would remain safe and effective.[86] However, there may be certain modifications to the indications for use that may be appropriate for inclusion in a PCCP, and are detailed further in the subsections below. FDA highly encourages manufacturers discuss modifications to the indications for use that may be included in a proposed PCCP with the appropriate FDA review division through the Q-Submission Program.

In the subsections below, FDA provides recommendations for how manufacturers should determine whether a modification may be appropriate for inclusion in a PCCP. We also provide some high-level examples of modifications that generally may be or are not appropriate for inclusion in a PCCP. However, the high-level examples are not exhaustive, and are not intended to cover all possible details, risks, or considerations. Ultimately, decisions about the types of modifications to be included in a PCCP are generally fact-specific for each device.

Recognizing there is a spectrum of risk for devices, for purposes of reviewing a PCCP, FDA intends to, among other considerations, take into account the Guiding Principles recommended in this guidance (Section IV.), the benefit-risk profile of the specific device that is the subject of the PCCP, the specific modifications being proposed, and FDA's experience applying this policy across different device types. As such, certain modifications that may be appropriate for inclusion in a PCCP for one device may not be appropriate for inclusion in a PCCP for another device. Some modifications may not be appropriate for inclusion within a PCCP for any device.

[83] See sections 515C(a)(2) and 515C(b)(2) of the FD&C Act.
[84] Section 515C(b)(2)(B) of the FD&C Act.
[85] FDA has a long-standing policy of applying the definition of indications for use in the PMA regulation at 21 CFR 814.20(b)(3)(i) in the same way in the 510(k) context. See the FDA guidance "The 510(k) Program: Evaluating Substantial Equivalence in Premarket Notifications [510(k)]."
[86] Sections 515C(a)(2) and 515C(b)(2)(A) of the FD&C Act.

A. Determining Whether a Modification may be Appropriate for Inclusion in a PCCP in a 510(k) or De Novo Submission

Pursuant to 21 CFR 807.81(a)(3), and as further described in FDA's guidances on "Deciding When to Submit a 510(k) for a Change to an Existing Device" and "Deciding When to Submit a 510(k) for a Software Change to an Existing Device" (referred to hereafter as "510(k) Modifications guidances"), "significant changes or modifications that require a [510(k)]" include "[a] change or modification that could significantly affect the safety or effectiveness of the device, e.g., a significant change or modification in design, material, chemical composition, energy source, or manufacturing process" or "[a] major change or modification in the intended use of the device." Consistent with section 515C(b)(2) of the FD&C Act, FDA "may clear a [PCCP] submitted in a [510(k)] that describes planned changes that may be made to the device (and that would otherwise require a new [510(k)]), if—(A) the device remains safe and effective without any such change; and (B) the device would remain substantially equivalent to the predicate."

Under section 515C(b)(2)(B) of the FD&C Act, FDA may clear a PCCP for planned changes that would otherwise require a new 510(k) if, among other things, the device remains substantially equivalent to the predicate. Under section 513(i)(1)(A) of the FD&C Act, substantial equivalence means, in part, that the device has the same intended use as the predicate device. Therefore, the modifications included in a PCCP must maintain the device within the device's intended use.[87] However, a significant change or modification in design, material, chemical composition, energy source, or manufacturing process may be appropriate for inclusion in a PCCP. As described in the 510(k) Modifications guidances, FDA recommends when assessing such types of modifications that a manufacturer should first conduct a risk-based assessment to determine whether the modification would require a new marketing submission,[88] and therefore whether that modification may be appropriate for inclusion in a PCCP. FDA recommends that manufacturers use the results of a risk-based assessment to help categorize modifications by those that could introduce new risks or those that could significantly modify existing risks.

Accordingly, modifications that could introduce a new risk are those that could introduce a new hazard or hazardous situations that did not exist for the original device and for which the pre-mitigation risk level associated with the new risk is not considered to be acceptable. Modifications that could introduce new risks are generally not appropriate for inclusion in a PCCP because the risks of implementing the modification are likely not adequately mitigated by the existing risk management framework of the device and the manufacturer's quality system.

Modifications that could significantly modify an existing risk are those that could change the risk score, risk acceptability category, or duration of risk. Modifications that could significantly modify existing risks generally may be appropriate for inclusion in a PCCP when the risks of implementing the modification are adequately mitigated by the existing risk management

[87] Section 515C(b)(2) of the FD&C Act.
[88] 21 CFR 807.81(a)(3) and 21 CFR 814.39(a).

framework of the device and the manufacturer's quality system. For additional information on whether a modification could introduce a new risk or significantly change an existing risk, see the 510(k) Modifications guidances.

To harmonize with our policy for device modifications for devices subject to 510(k) or De Novo requirements, FDA recommends using the following process (see Figure 2) to determine whether a modification may be appropriate for inclusion in a PCCP. We recommend that the process depicted in Figure 2 be considered in conjunction with the recommendations in this guidance, as there are many factors to consider in concert to determine whether a modification may be appropriate for inclusion in a PCCP.

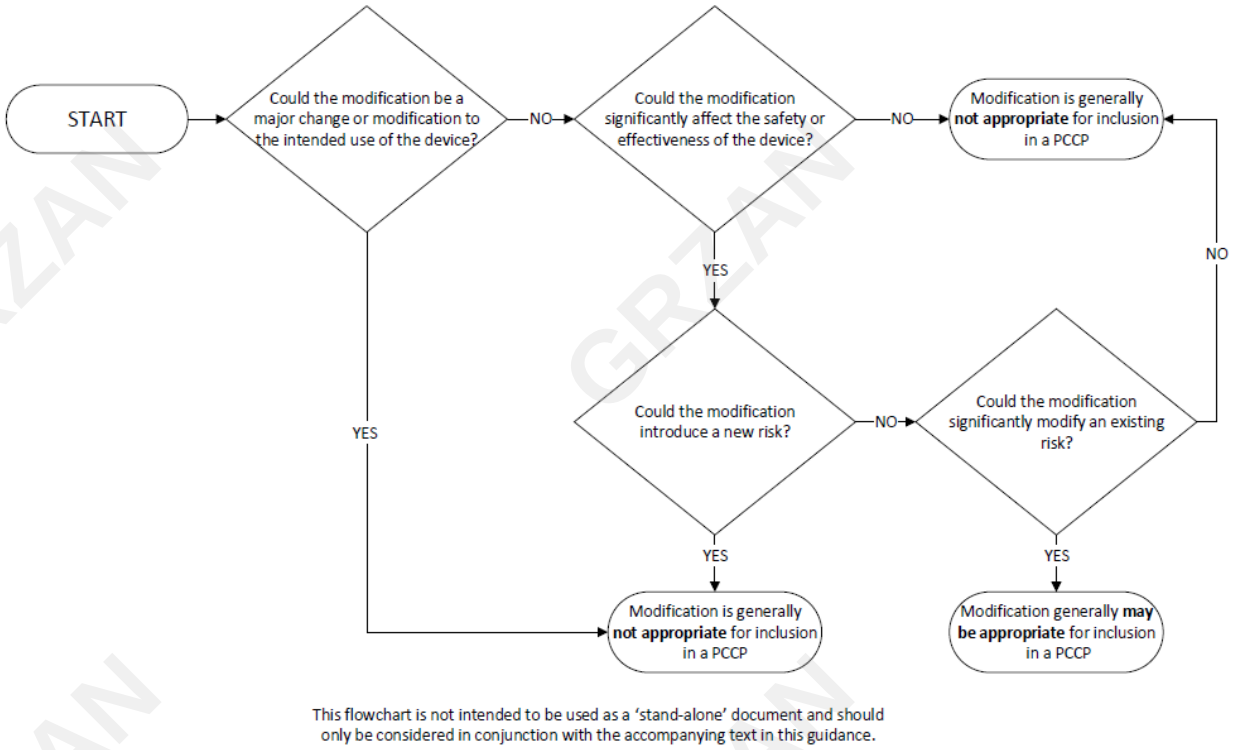


Figure 2. Determining Whether a Modification may be Appropriate for Inclusion in a PCCP for a 510(k) or De Novo Device

Please see below for lists of certain high-level modifications that generally may be appropriate or are not appropriate for inclusion in a PCCP. To avoid misinterpretation, we recommend that the lists be considered together to determine the appropriateness of including a modification in a PCCP. For example, a change in materials may be appropriate to include in a PCCP, however, if such a change may need new clinical data, it would not be appropriate to include in a PCCP.

Modifications that generally may be appropriate for inclusion in a PCCP:

- Certain changes in device design, including dimensions, performance specifications, wireless communication, components or accessories, or the patient/user interface

- Change in sterilization, packaging, transport, or expiration dating using well-established methods
- Certain changes in materials/components (e.g., different raw materials, reagents, or hardware components)
- Certain changes in software related to device compatibility and/or interoperability (e.g., changes to support device use on additional operating system(s), new data vendors and/or sources, or compatibility with additional devices)
- Certain changes in software consistent with the intended use to improve device performance
- Certain changes to the labeling to describe a specific subset of a patient population within the originally indicated patient population that the device is intended for use in diagnosing, treating, preventing, curing, or mitigating
- Certain changes in the labeling and/or the indications for use to specify use of the device with an additional device, component, or human genetic variant
- Certain changes in the indications for use regarding use in the home setting

Modifications that are generally <u>not appropriate</u> for inclusion in a PCCP:

- Change to device control mechanism, operating principle, or energy type
- Change in device design that could affect the intended use of the device
- Change from a device labeled for single use only to a device labeled as reusable
- Change to or removal of contraindications
- Change from prescription to over-the-counter use
- Changes from "general to specific"[89]
- Change in the labeling and/or the indications for use to include a new patient population
- Changes that may need new clinical data[90]
- Change to address a recall or safety issue
- Change to a device constituent part that impacts the biologic or drug constituent part

B. Determining Whether a Modification may be Appropriate for Inclusion in a PCCP in a PMA Application or Supplement

Pursuant to section 515(d)(5)(A)(i) of the FD&C Act and 21 CFR 814.39(a), and as further described in FDA's guidance on "Modifications to Devices Subject to Premarket Approval (PMA) - The PMA Supplement Decision-Making Process" (referred to hereafter as the "PMA Modifications guidance"), "[a]fter FDA's approval of a PMA, an applicant shall submit a PMA supplement for review and approval by FDA before making a change affecting the safety or

[89] A change from "general to specific", i.e., a change from general to a specific indications for use, is any proposed increase in the level of specificity of the indication for use of a medical device. For additional information, see FDA's guidance "General/Specific Intended Use."

[90] Certain changes that may need new clinical data, such as method comparison data for IVDs, may be appropriate for inclusion in a PCCP.

effectiveness of the device for which the applicant has an approved PMA" unless an exception applies. Consistent with section 515C(a)(2) of the FD&C Act, FDA "may approve a [PCCP] submitted in an application, including a supplemental application, under section 515 that describes planned changes that may be made to the device (and that would otherwise require a supplemental application under section 515), if the device remains safe and effective without any change."

Under section 515C(a)(2) of the FD&C Act, FDA may approve a PCCP for planned changes that would otherwise require a supplemental application under section 515 of the FD&C Act. Therefore, the modifications included in a PCCP must maintain the device within the device's intended use.[91] Other modifications that could affect the safety or effectiveness of the device may be appropriate for inclusion in a PCCP.

Minor changes and manufacturing changes are two types of modifications that could affect the safety or effectiveness of the device. A modification is considered a minor change if it is a minor change to the design of the device, software, sterilization, or labeling, typically otherwise reviewed under a real-time supplement.[92] A modification is a manufacturing change if it is a modification to the manufacturing procedures or methods of manufacture affecting the safety or effectiveness of the device, typically otherwise reviewed under a 30-day notice.[93]

Accordingly, modifications that are minor changes or manufacturing changes generally may be appropriate for inclusion in a PCCP when the risks of implementing the modification are adequately mitigated by the existing risk management framework of the device and the manufacturer's quality system. Conversely, modifications that are not minor changes or manufacturing changes are generally not appropriate for inclusion in a PCCP because the risks of implementing the modification are likely not adequately mitigated by the existing risk management framework of the device and the manufacturer's quality system.

To harmonize with our policy for device modifications for devices subject to PMA requirements, FDA recommends using the following process (see Figure 3) to determine whether a modification may be appropriate for inclusion in a PCCP. We recommend that the process depicted in Figure 3 be considered in conjunction with the recommendations in this guidance, as there are many factors to consider in concert to determine whether a modification may be appropriate for inclusion in a PCCP.

[91] See section 515C(a)(2) of the FD&C Act.
[92] See section 737(4)(D) of the FD&C Act.
[93] See section 737(5) of the FD&C Act.

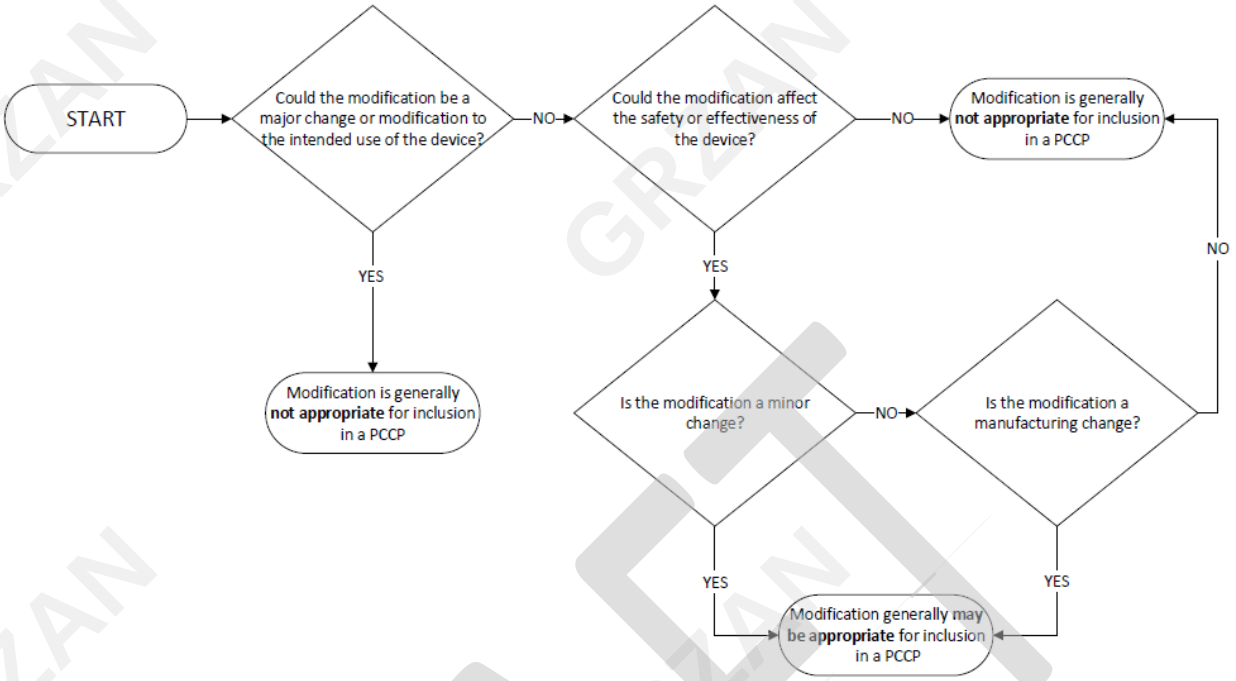


Figure 3. Determining Whether a Modification may be Appropriate for Inclusion in a PCCP for a PMA Device

Please see below for lists of certain high-level modifications that generally may be appropriate or are not appropriate for inclusion in a PCCP. To avoid misinterpretation, we recommend that the lists be considered together to determine the appropriateness of including a modification in a PCCP. For example, a minor change in the instructions for use in the labeling may be appropriate to include in a PCCP, however, if such a change addresses a safety issue, it would not be appropriate to include in a PCCP.

Modifications that generally may be appropriate for inclusion in a PCCP:

- Minor change in device design, including dimensions, performance specifications, wireless communication, components or accessories, or the patient/user interface
- Minor change in sterilization, packaging, transport, or expiration dating
- Minor change in a material/component that has similar technical specifications to those for the authorized device (e.g., different source or supplier for raw materials, reagents, or hardware components)
- Minor change in software related to device compatibility and/or interoperability (e.g., changes to support device use on upgraded operating system(s) or new data vendors and/or sources)
- Minor change in software consistent with the intended use to improve device performance

- Minor change to the labeling to describe a specific subset of a patient population within the originally indicated patient population that the device is intended for use in diagnosing, treating, preventing, curing, or mitigating
- Minor change to the labeling, including instructions for use, warnings, precautions, or other labeling that does not affect the indications for use or contraindications
- Minor change in the labeling and/or the indications for use to specify use of the device with an additional device, component, or human genetic variant
- Certain changes in manufacturing procedures:
    - Change to sterilization, joining, or cleaning procedures
    - Change to automate existing processes
    - Change to environmental conditions of manufacturing, storage, or distribution facilities (e.g., addition/relocation of a room for manufacturing purposes to the existing manufacturing space)
- Certain changes in methods of manufacture:
    - Change in manufacturing materials (e.g., new/different machine lubricants)
    - Change in manufacturing software
    - Change in supplier for manufacturing components where specifications are unchanged (e.g., addition of a raw material supplier for materials critical to the performance of the device)

Modifications that are generally <u>not appropriate</u> for inclusion in a PCCP:

- Significant change to components, materials, design, specifications, software, or color additives, such as:
    - Change to device control mechanism, operating principle, or energy type
    - Change in device design that could affect the intended use of the device
- Significant change in labeling, such as:
    - Change from a device labeled for single use only to a device labeled as reusable
    - Changes from "general to specific"[94]
    - Change to or removal of contraindications
- Change in the labeling and/or the indications for use to include a new patient population
- Changes that may need new clinical data[95]
- Change to address a recall or safety issue
- Change to a device constituent part that impacts the biologic or drug constituent part
- Change to add, expand, or move the manufacturing or sterilization site of a finished device

VII. Recommended Content for a PCCP

A. Description of Modifications

[94] See footnote 89.
[95] See footnote 90.

A description of each planned modification to a device should be included in the Description of Modifications section of a PCCP. The detailed description should describe specific changes to the device characteristics and performance resulting from implementation of the modifications. To ensure an efficient review, FDA recommends that a PCCP include only a limited number of modifications that are specific, and that can be verified and validated.

(1) Goals of the Description of Modifications

A dedicated Description of Modifications section in a PCCP should identify the specific, planned modifications to the device that the manufacturer intends to implement. The Description of Modifications should include the specifications for the characteristics and performance of the device that, following the agreed upon verification and validation described in the Modification Protocol, can be implemented without a new marketing submission.

(2) Content of the Description of Modifications

To achieve these goals, FDA recommends that the Description of Modifications enumerate the list of individual proposed device modifications discussed in the PCCP, as well as the specific rationale for the change to each part of the device that is planned to be modified. In some situations, a Description of Modifications may consist of multiple modifications. It may be helpful to reference the labeling sections that are anticipated to be impacted for each modification in the Description of Modifications section (such labeling changes should be included in the Modification Protocol, as described in Section VII.B.(2)b. of this guidance).

FDA recommends that a PCCP include modifications that are specific, and that can be verified and validated. Modifications should also be presented at a level of detail that permits understanding of the specific modifications that will be made to the device. Each modification should be linked to a specific performance evaluation activity within the Modification Protocol (for an example, see Table 1 in Section VII.C. of this guidance).

B. Modification Protocol

The Modification Protocol should include the documentation describing the methods that will be followed when developing, validating, and implementing modifications delineated in the Description of Modifications section of the PCCP. The Modification Protocol should also include the verification and validation activities, including pre-defined acceptance criteria, for those modifications, and a step-by-step delineation of how those modifications will be implemented while assuring the device remains safe and effective.

Documentation of modifications verified and validated per the Modification Protocol must be compliant with the QSR, including that the manufacturer must document the change in accordance with the manufacturer's quality system.[96] The QSR requires manufacturers of finished medical devices to review and approve modifications to device design and production

[96] 21 CFR Part 820.

(21 CFR 820.30(i) and 820.70(b)) and document changes and approvals in the device master record (21 CFR 820.181).

(1) Goals of the Modification Protocol

Whereas the Description of Modifications outlines the planned modifications to a device, the Modification Protocol should describe the methods that will be followed when developing, validating, and implementing those modifications to ensure the device remains safe and effective. The methods described in the Modification Protocol should be consistent with and support the modifications outlined in the Description of Modifications.

The goals of the Modification Protocol are to:

- Identify the appropriate and applicable data, test methods, analysis methods, and specified acceptance criteria used to develop, validate, and implement all proposed modifications;
- Identify the update process, and as appropriate, the plans for communication and/or training for users for implemented modifications;
- Ensure that the information that would otherwise be generated and submitted to FDA (i.e., if the modifications were implemented on a device that did not have an authorized PCCP) will be generated by the manufacturer for each modification and maintained consistent with recordkeeping requirements and in accordance with the manufacturer's quality system;[97]
- Ensure that anticipated risks and risk mitigation strategies have been identified and included in the Impact Assessment; and
- Be least burdensome[98] for the manufacturer to develop and for FDA to review. This includes being traceable (so that modifications in the Description of Modifications can be traced to verification and validation activities in the Modification Protocol) and specific (so that the PCCP is sufficiently comprehensive to support the proposed modifications).

Manufacturers should follow their risk management processes to develop a Modification Protocol that considers each modification. In some cases, the same methods described in the Modification Protocol may support all modifications in a PCCP for a device. In other cases, the same methods described in the Modification Protocol may not be adequate for every modification in a PCCP. For each planned modification provided in the Description of Modifications, FDA recommends that the information outlined in this section be addressed in a Modification Protocol. The Modification Protocol should include a description of how its proposed methods are similar to or different from methods used elsewhere in the marketing submission. For example, if the validation methods in the Modification Protocol represent a subset of the original testing for the device, or if the acceptance criteria for the validation are different, manufacturers should describe these differences and provide a justification. The

[97] 21 CFR Part 820.

[98] See FDA's guidance "The Least Burdensome Provisions: Concept and Principles."

justification for a different methodology may include references to other marketing submissions where the methodology was used for similar modifications.

(2) Content of the Modification Protocol Section

To achieve these goals, FDA recommends that a Modification Protocol include information regarding the manufacturer's performance evaluation methods, and also, when appropriate, update procedures. In FDA's experience, this is generally the type of information that will enable FDA to evaluate the PCCP. For a particular marketing submission, additional information in a Modification Protocol may need to be included to assist in FDA's determination of substantial equivalence or reasonable assurance of safety and effectiveness of the device and PCCP.

a. Performance Evaluation Methods

Performance evaluation of the device is important to ensure that specified acceptance criteria for all proposed modifications will continue to be met for the device's specifications. FDA may require that performance requirements for changes made under the plan be provided in a PCCP.[99] Performance evaluation methods should include the plans to verify and validate that the modified device will meet the specifications identified as part of a specific modification, in addition to maintaining the specifications that are not part of the modification, but may be impacted by the modification. Performance evaluation should include, as applicable, the plans for verification and validation of the entire device following the implementation of each individual modification and in aggregate for the planned modifications. In general, depending on the proposed modifications, this information may be similar to the performance evaluation methods used to support the original marketing submission for the device. The content of this section in a Modification Protocol should provide details on the study design, performance metrics, pre-defined acceptance criteria, and statistical tests for each planned modification. More comprehensive testing can potentially support a broader set of proposed modifications.

To determine the information that manufacturers should provide in a Modification Protocol, FDA recommends considering the specific, planned modifications to your device and reviewing FDA guidances, including, but not limited to:

- Device-specific guidance[100] that may be applicable to your device;
- Performance testing guidances, such as those on non-clinical bench performance testing or analytical studies[101] and non-clinical animal performance testing,[102,103]; and

[99] See sections 515C(a)(3), 515C(b)(3), and 513(f)(2) of the FD&C Act.
[100] See FDA's guidance search database.
[101] See, e.g., FDA's guidance on "Recommended Content and Format of Non-Clinical Bench Performance Testing Information in Premarket Submissions."
[102] FDA supports the principles of the "3Rs," to replace, reduce, and/or refine animal use in testing, when feasible. We encourage manufacturers to consult with FDA if they wish to use a non-animal testing method that they believe is suitable, adequate, validated, and feasible. We will consider if a proposed alternative method could be assessed for equivalency to an animal test method.
[103] See, e.g., FDA's guidance on "General Considerations for Animal Studies Intended to Evaluate Medical Devices."

- Other horizontal, cross-cutting guidances (e.g., biocompatibility or electromagnetic compatibility).

The Modification Protocol should also affirmatively state that if there is an unresolvable failure in performance evaluation for a specific modification (e.g., the predefined acceptance criteria for a specific modification are not met), the failure(s) will be recorded, and the specific modification(s) will not be implemented. A failure would not be considered to be unresolvable if a root cause analysis of the failure reveals it is not related to specific aspects of the PCCP, and in such cases, performance testing may be conducted again.

b. Update Procedures

FDA recommends that a Modification Protocol include information on update procedures. The update procedures in a Modification Protocol should describe how manufacturers will update their devices to implement the modifications consistent with QSR, and, if appropriate for such modifications, provide appropriate transparency to users and updated user training.[104] The manufacturer should also describe their post-market surveillance plans and procedures, which may include real-world monitoring and notification requirements if the device does not function as intended pursuant to the authorized PCCP.[105] As part of a manufacturer's responsibility to ensure that devices remain safe and effective, FDA anticipates that manufacturers will monitor their device's safety (e.g., adverse events) and effectiveness (e.g., performance) over time as modifications are implemented consistent with their authorized PCCP.

The update procedures in a Modification Protocol should also address how labeling will be updated when modifications are implemented, as appropriate.[106] It should also include a description of the labeling sections that are anticipated to be impacted by the implementation of the modifications. The available labeling must include adequate directions for use.[107] The available labeling should also reflect information about the current version(s) of the device available to the user. New unique device identifiers (UDIs) are required for devices that are required to bear a UDI on its label when there is a new version and/or model, and for new device packages.[108] FDA recommends that the labeling not include information on modifications to the device that have not been implemented in the available version because it could cause confusion and would be misleading. Additionally, if the labeling states that a modification to the device has been implemented when it has not, the device might be deemed misbranded.[109]

[104] See sections 515C(a)(3), 515C(b)(3), and 513(f)(2) of the FD&C Act.
[105] See sections 515C(a)(3), 515C(b)(3), and 513(f)(2) of the FD&C Act.
[106] See Section V.C. of this guidance for the recommendations regarding information about the PCCP that should be included in the device labeling.
[107] See 21 CFR 801.5(a), requiring that labeling include adequate directions for use including statements of all conditions, purposes, or uses for which the device is intended.
[108] See 21 CFR 830.50.
[109] See section 502(a)(1) of the FD&C Act, stating that a medical device is deemed misbranded if its labeling is false or misleading in any particular.

C. Traceability Between the Description of Modifications Section and the Modification Protocol Section

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 below in Table 1. This sample traceability table provides an example of how a manufacturer can depict the traceability between the Description of Modifications and Modification Protocol, as well as how to provide clear references to where within the PCCP this information is located in a marketing submission. In other words, a traceability table can help to identify where each method supporting each modification may be found in the marketing submission.

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

Modification Protocol Component		
Modification	Performance Evaluation Methods	Update Procedures
Modification #1	*Method A (see Section X.A)*	*Method J (see Section X.J)*
Modification #2	*Method A (see Section X.A)*	*Method K (see Section X.K)*
Modification #3	*Method B (see Section X.B)*	*Method L (see Section X.L)*

D. Impact Assessment

An Impact Assessment in a PCCP is the documentation of the assessment of the benefits and risks of implementing a PCCP for a device, as well as the mitigations of those risks. The manufacturer's existing quality system should be used as the framework in which to conduct an Impact Assessment for the modifications set forth in the PCCP.

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

1) Compare the version of the device with each modification implemented individually to the version of the device without any modifications implemented;

2) Discuss the benefits and risks, including risks of harm,[110] of each individual modification;
3) Discuss how the verification and validation activities proposed within the Modification Protocol continue to reasonably ensure the safety and effectiveness of the device;
4) Discuss how the implementation of one modification impacts the implementation of another; and
5) Describe the cumulative impact of implementing all modifications.

FDA believes it is important to address these elements in an Impact Assessment in order to demonstrate that the combination of the proposed modifications is unlikely to introduce additional, unmitigated risks, and that the safety and effectiveness of the device is maintained as modifications are implemented.

Impact Assessment documentation for a PCCP in a marketing submission should also 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, such documentation should also discuss how the individual modifications included in the PCCP for the device constituent part impact the biologic and/or drug constituent part, and the combination product as a whole. Additionally, if the modifications in a PCCP are intended to affect any device functions of a multiple function device product, we recommend considering FDA's guidance "Multiple Function Device Products: Policy and Considerations." In particular, as it pertains to the device and the PCCP, it is important to determine if any information should be included in the Impact Assessment in a PCCP in a marketing submission so that FDA may assess the impact of the "other function(s)" on the safety or effectiveness of the device as it is modified consistent with the PCCP.

Some information related to the Impact Assessment may be included elsewhere in your marketing submission, for example in sections for the risk assessment for the device or the Modification Protocol in your PCCP. As such, FDA recommends providing clear references in your Impact Assessment to the relevant sections in your marketing submission that support the Impact Assessment.

VIII. Examples of Modifications for PCCPs

This section includes illustrative examples of modifications that generally may be or are not appropriate for inclusion in a PCCP for a specific device. Each example begins with a brief description of a device and a statement about a proposed modification for inclusion in a PCCP. Please note that the provided summaries of the devices and modifications in this section are not intended to reflect the complete content or detail expected in a Description of Modifications section in a PCCP. Rather, proposed modifications should be described in much greater detail in a PCCP, consistent with the recommendations provided throughout this guidance. Due to the

[110] See, e.g., harm, as defined in ISO 14971 *Medical devices – Application of risk management to medical devices*, is the physical injury or damage to the health of people.

complexity of devices and PCCPs, it is not practical to describe all relevant considerations, or a complete PCCP, for the limited examples presented below.

As previously stated, recognizing there is a spectrum of risks for devices, for purposes of reviewing a PCCP, FDA intends to, among other considerations, take into account the Guiding Principles recommended in this guidance (Section IV.), the benefit-risk profile of the specific device that is the subject of the PCCP, the specific modifications being proposed, and FDA's experience applying this policy across different device types. As such, certain modifications that may be appropriate for inclusion in a PCCP for one device may not be appropriate for inclusion in a PCCP for another device. Some modifications may not be appropriate for inclusion within a PCCP for any device.

FDA encourages manufacturers to leverage the Q-Submission Program to obtain FDA feedback on a proposed PCCP for a device and submission type prior to submitting a marketing submission.

Example 1

This device is a microarray-based IVD cancer predisposition risk assessment system for over-the-counter use that is intended to detect 5 single nucleotide variants in BRCA1 and 3 single nucleotide variants in BRCA2 in saliva for the purposes of describing if a person is at increased risk of breast cancer, ovarian cancer, or prostate cancer.

Modifications that generally may be appropriate for inclusion in a PCCP:

- Addition of new single nucleotide variants
- Addition of insertion and deletion variants up to 20 base pairs
- Updates to the labeling that inform potential cross-reactive polymorphisms

Modifications that are generally not appropriate for inclusion in a PCCP:

- Addition of copy number variants
- Addition of a new gene
- Change in the collection device and sample type (e.g., saliva to buccal swab)
- Change from manual to automated process (e.g., for sample dilution)

Example 2

This device is an ion selective electrode IVD intended for use on a laboratory-based chemistry analyzer to quantify the concentrations of potassium ions in serum samples for the purposes of monitoring electrolyte balance in the diagnosis and treatment of diseases and conditions characterized by low or high blood potassium levels.

Modifications that generally may be appropriate for inclusion in a PCCP:

- Addition of lithium heparin plasma as a sample type
- Extension of sample stability claims (e.g., 2 hours at room temperature to 4 hours at room temperature)

- Addition of a new potassium ion selective electrode

Modifications that are generally not appropriate for inclusion in a PCCP:

- Addition of urine or capillary whole blood as a sample type
- Addition of at-home sample collection
- Addition of point of care use

Example 3

This device is a non-absorbable polyethylene surgical suture intended for soft tissue approximation or ligation.

Modifications that generally may be appropriate for inclusion in a PCCP:

- Change to a different non-novel sterilization method (e.g., Established Category A to Established Category B sterilization method[111])
- Extend shelf life using a different well-established method than what was provided for the initial shelf life testing
- Addition of sutures to the product line with different dimensions that are within the range of dimensions of those currently authorized
- Addition of dye with an appropriate FDA listed color additive per 21 CFR Part 74 Subpart D[112]

Modifications that are generally not appropriate for inclusion in a PCCP:

- Addition of antimicrobials
- Change in filament design to an atypical design (e.g., unique braiding patterns, anchors, or knots)
- Addition of a stiffening agent to the ends of the suture to address a recall

Example 4

This device is a multi-parameter physiological patient monitor with arrhythmia detection and alarms for use in a hospital environment.

Modifications that generally may be appropriate for inclusion in a PCCP:

- Hardware and software updates to introduce compatibility with a newly cleared monitoring parameter/module
- Change to a new wireless card that has different technical specifications than those for the authorized device

[111] See FDA's guidance "Submission and Review of Sterility Information in Premarket Notification (510(k)) Submissions for Devices Labeled as Sterile."

[112] For additional information on color additives, see FDA's website on "Summary of Color Additives for Use in the United States in Foods, Drugs, Cosmetics, and Medical Devices."

- Change to the software to upgrade to a new version of the currently supported operating system (OS) on the basis of a risk assessment that shows changes between major OS versions could significantly impact the software's performance
- Change to the visualization of patient monitoring data (e.g., heart rate) in the user interface
- Addition of new parameter trend graphs for use in active patient monitoring

Modifications that are generally not appropriate for inclusion in a PCCP:

- Addition of a new physiological parameter to be monitored (e.g., blood oxygen level, temperature)
- Addition of a novel physiological or predictive index or algorithm (e.g., new algorithm to predict risk of patient deterioration)
- Significant changes to the alarm architecture
- Significant changes to the design of the printed circuit board

Example 5

This device is an over-the-counter mobile medical app intended to assess risk of moderate to severe obstructive sleep apnea.

Modifications that generally may be appropriate for inclusion in a PCCP:

- Addition of new connected data sources to provide the same types of inputs needed by the app
- Addition of support for mobile platforms with different operating systems, where app performance specifications have been retained (e.g., introducing an iOS version of an Android app)
- Change in software algorithm to improve device performance by reducing false positive outputs in typical use based on additional real-world use data

Modifications that are generally not appropriate for inclusion in a PCCP:

- Addition of an alternate type of input data on which the app will make or refine its assessment of sleep apnea risk
- Significant change to software architecture
- Change in labeling to include claims about helping users to assess risk of mild obstructive sleep apnea

Example 6

This device is an IVD intended for use in determining quantitative susceptibility of Candida species to Caspofungin.

Modifications that generally may be appropriate for inclusion in a PCCP:

- Plans for future updates to breakpoints that are consistent with FDA's website on FDA-Recognized Antimicrobial Susceptibility Test Interpretive Criteria, consistent with the

recommendations in FDA's guidance "Antimicrobial Susceptibility Test (AST) System Devices – Updating Breakpoints in Device Labeling"

Modifications that are generally not appropriate for inclusion in a PCCP:

- Addition of a new drug to test Candida species
- Addition of claimed organism species not included in the original authorized device
- Addition of alternative reading method (e.g., from manual (visual/turbidimetric or colorimetric) to automated (fluorescence))
- Addition of alternative inoculation method (e.g., from manual to automated)

Example 7

This device is a human leukocyte antigen (HLA) molecular typing assay intended to aid donor and recipient matching in transplantation and transfusion. It uses polymerase chain reaction sequence-specific primer (PCR-SSP) or sequence-specific oligonucleotide probes (SSOP) to detect HLA-B alleles.

Modifications that generally may be appropriate for inclusion in a PCCP:

- Addition of new primers or probes to detect new HLA-B alleles
- Updates to the data analysis software to resolve or inform HLA typing ambiguities based on an internationally recognized HLA sequence database

Modifications that are generally not appropriate for inclusion in a PCCP:

- Addition of new primers or probes to detect alleles of a different HLA gene or locus
- Change in the indications for use to include a companion diagnostic claim to identify patients who have specific HLA allele(s) and may benefit from treatment with a corresponding therapeutic product or are likely to be at increased risk for serious adverse reactions as a result of treatment with a corresponding therapeutic product

Example 8

This device is an implantable pulse generator pacemaker.

Modifications that generally may be appropriate for inclusion in a PCCP:

- Addition of an alternate component supplier (e.g., memory chip, resistor, capacitor) where the component specifications and design requirements are identical to those of the currently approved component
- Minor software changes to improve the battery longevity estimation algorithm
- Minor change to the wireless modem in the pacemaker to expand the range of cellular frequencies and bands
- An update to change the Magnetic Resonance (MR) labeling for a particular device model from MR Unsafe to MR Conditional based on well-established test methods and acceptance criteria

Modifications that are generally not appropriate for inclusion in a PCCP:

- A manufacturing change to an adhesive application process step made in response to reported device failure events of premature battery depletion due to an identified process variation
- Addition of a new battery design or change to the battery chemistry
- Addition of a new software feature to optimize therapy delivery by customizing pacing parameters
- Change to device software to address reports of failure to deliver pacing therapy due to sensing errors
- Change to the indications for use to include conduction system pacing

Example 9

This device is an immunoassay-based IVD intended to quantitatively measure prostate specific antigen in serum to aid in the detection of prostate cancer in conjunction with a digital rectal exam.

Modifications that generally may be appropriate for inclusion in a PCCP:

- Addition of lithium heparin plasma as a sample type
- A protocol for extension of sample stability claims
- Drug interference for the alkaline phosphatase detection mechanism that does not require a design change to address the interference
- Addition of an alternate antibody supplier where the specifications for the antibody are identical to those of the currently approved antibody
- In-processing manufacturing change (e.g., reagent pooling) to add a filling suite within the same building

Modifications that generally would not be appropriate for inclusion in a PCCP:

- Addition of capillary whole blood as a sample type
- Addition of point-of-care use
- Change to remove use of the test in conjunction with a digital rectal exam

Example 10

This device is a coronary drug-eluting stent system, which is a device-led combination product. The stent is coated with a sirolimus/polymer blend intended to inhibit restenosis.

Modifications that generally may be appropriate for inclusion in a PCCP:

- Addition of an alternate delivery system component supplier (e.g., hypotube, adhesive) where the component specifications and design requirements are identical to those of the currently approved component
- Addition of stent systems to the product line with different dimensions, but otherwise identical designs, that are within the range of dimensions of those currently authorized, which uses identical manufacturing processes

- Automation of a dimension measurement inspection process step in manufacturing

Modifications that generally would not be appropriate for inclusion in a PCCP:

- Change in the composition of the drug coating (e.g., a change from sirolimus to a different drug, a change in the concentration or total dose of sirolimus, or a change in the ratio of polymer to sirolimus)
- A manufacturing change that impacts the drug coating (e.g., a change in the materials or methods used to filter the coating solution)
- Change in the labeling to increase the post-dilation expansion limit of the stent
- Change in the labeling to include new indications, instructions, guidance, or clinical information regarding use in a new patient population (e.g., adding the results of a clinical study of the device's use in patients with complex coronary lesions)

IX. Sample of 510(k) Summary Information Regarding the PCCP

This section includes a sample of 510(k) summary information regarding a PCCP for a device that was authorized with a PCCP. It is based on some of the modifications included in Example 4 in Section VIII. of this guidance. For complete information on the 510(k) summary, see 21 CFR 807.92, and FDA's "The 510(k) Program: Evaluating Substantial Equivalence in Premarket Notifications [510(k)]" guidance, including Appendices B. and C.

Predetermined change control plan

The predetermined change control plan (PCCP) for the device specifies anticipated modifications to the device software to add a new wireless card and to upgrade the device's operating system. The PCCP also specifies the methods to implement those modifications so that the device remains as safe and as effective as the predicate device. The detailed description of the modifications, testing methods, validation activities, performance requirements, and communication to users are summarized in the table below.

Planned Modifications	Test Methods and Validation Activities	Communication to users, as needed
Addition of a new wireless card	Testing for basic safety and essential performance will be repeated according to FDA-recognized editions of the following voluntary consensus standards: • ANSI/AAMI ES60601-1 • IEC 60601-1-2 • IEC 60601-1-8 • IEC 60601-4-2 • AIM 7351731 • IEEE/ANSI C63.27 • AAMI TIR69 Test methods will follow the recommendations in the most recent version of the following FDA guidances: • "Electromagnetic Compatibility (EMC) of Medical Devices" • "Radio Frequency Wireless Technology in Medical Devices"	Labeling will be updated in accordance with the authorized PCCP to provide users with current information regarding the device's wireless capabilities
Upgrade to device operating system	Verified and validated by the requirements of the Modification Protocol, including necessary regression testing	Users will be notified of software updates (including any user instructions for the update process) in accordance with the authorized PCCP Labeling will be updated in accordance with the authorized PCCP to provide users with current information regarding the device's upgraded operating system

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