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Client Alert

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Predetermined Change Control Plans (PCCPs) for Medical Devices: FDA Issues Draft Guidance

On August 22, 2024, the U.S. Food and Drug Administration (FDA or Agency) issued a draft guidance entitled, *Predetermined Change Control Plans for Medical Devices*. The draft guidance describes how FDA plans to implement new section 515C(a)-(c) of the Federal Food, Drug, and Cosmetic Act (FD&C Act), which authorizes FDA to clear or approve predetermined change control plans (PCCPs). With a PCCP, a device manufacturer may obtain advance clearance or approval of planned modifications to a device that would otherwise have required a new 510(k) or premarket approval (PMA) supplement.

The PCCP authority is broad and applies to all types of medical devices. It is available both for new devices and for those that already have an existing 510(k) clearance or PMA approval. It is even available for the device constituent of device-led combination products.

The new draft guidance suggests that FDA is committed to embracing its PCCP authority. If this pathway proves viable, it could dramatically increase the tempo of innovation in the medical device industry. It would allow manufacturers to obtain marketing authorization from FDA for new features and iterations in parallel with the development process, thus shaving many months off time to market for modifications made after the initial submission authorizing the PCCP. If applied continuously over a device's life cycle, the time savings could be measured in years.

Although the concept of communicating predetermined changes to FDA has existed for several years, the term "PCCP" was introduced by the Agency in a 2019 discussion paper entitled, "Proposed Regulatory Framework for Modifications to Artificial Intelligence/Machine Learning (AI/ML)-Based Software as a Medical Device (SaMD)." Then, on

December 29, 2022, Congress added section 515C to the FD&C Act—authorizing FDA to clear and approve PCCPs—when it enacted an amendment commonly known as "FDORA."[i] In April 2023, FDA published "Marketing Submission Recommendations for a Predetermined Change Control Plan for Artificial Intelligence/Machine Learning (AI/ML)-Enabled Device Software Functions" as a draft guidance. Lessons learned from FDA's review of PCCPs related to AI/ML-enabled medical devices since that time have been incorporated into this draft guidance (*e.g.*, the emphasis on detail in the "Description of Modifications" section of the PCCP).

The new draft guidance applies to all types of medical devices, including Software as a Medical Device (SaMD) or Software in a Medical Device (SiMD) that does not incorporate AI/ML-enabled device software functions.

We recommend that manufacturers review their product portfolios to evaluate whether they have products that could benefit from advanced authorization of planned modifications. In the discussion below, we summarize the key points of the draft guidance. Additionally, FDA is holding a webinar on the draft guidance on September 3, 2024.

NEW SECTION 515C

Under Section 515C of the FD&C Act, FDA may clear or approve a PCCP that describes planned changes to a device, so long as the device remains safe and effective and, for Class I or II devices, substantially equivalent to the predicate device. When a manufacturer subsequently modifies the device, a new 510(k) or PMA supplement will not be required, so long as the changes are consistent with the previously cleared or approved PCCP.

Section 515C authorizes FDA to require that a change control plan include (i) labeling that ensures safe and effective use of the device as the device or its changes pursuant to its PCCP, (ii) notification requirements if the device does not function as intended pursuant to such plan, and (iii) performance requirements for changes made under the plan.

GUIDING PRINCIPLES FOR PCCPS[ii]

The draft guidance begins with general guiding principles. First, FDA emphasizes that devices with PCCPs must still meet the statutory standard of reasonable assurance of safety and effectiveness, including substantial equivalence for 510(k)-cleared devices. That fact implies that there must be sufficient information in a PCCP for FDA to make this finding.

Second, although a PCCP is optional for industry, FDA acknowledges that it may in some cases be the least burdensome approach to clearance. That is a fascinating and helpful point that sponsors can use to justify a PCCP.

Third, every PCCP is considered part of the marketing authorization and will be part of the device's letter of authorization, if the device is cleared or approved.

Fourth, the PCCP is specific. By this, FDA means that 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."

Fifth, PCCPs harmonize with existing FDA guidance regarding when a modification requires a new submission. This makes sense, because the statutory and regulatory standards for when a modification requires a new submission are not changed by the PCCP option.

COMPONENTS OF A PCCP[iii]

According to FDA, a PCCP should consist of a detailed Description of Modifications, a Modification Protocol, and an Impact Assessment. The detailed Description of Modifications should outline the specific, planned modifications that

may be made to the device, including the specifications for the characteristics and performance of the planned modifications. The Modification Protocol should describe the verification and validation activities, including pre-defined acceptance criteria, which will support each modification to assure the device remains safe and effective across the intended use populations. The Impact Assessment identifies the benefits and risks introduced by the 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.

ESTABLISHING A PCCP[iv]

A PCCP must be established through the PMA pathway, 510(k) pathway, or De Novo pathway, as appropriate, prior to implementing any modifications under that PCCP. FDA believes that a PCCP can be included in most types of PMAs and PMA supplements, both Traditional and Abbreviated 510(k)s, and De Novo Requests. It would not be appropriate to include a PCCP in a five-day "changes being effected" PMA supplement or a Special 510(k).

A question addressed by the draft guidance that is not explicitly addressed in FD&C Act section 515C is the role of the manufacturer's quality system. In the draft guidance, FDA emphasizes that PCCP modifications must be implemented in compliance with the Quality System Regulation (QSR), including risk management.[v] The Agency indicates that the manufacturing inspection conducted during a PMA review would need to be successful for approval of a PCCP. FDA acknowledges that, under FD&C Act section 513(f)(5), FDA may not condition 510(k) clearance on QSR compliance. The Agency, however, points to an exception in the statute that allows clearance to be withheld if there is "a substantial likelihood that the failure to comply with QSR will potentially present a serious risk to human health."[vi] FDA indicates that the Agency may withhold clearance of a PCCP on the basis of such a finding.

Under FDCA section 515C(c), a device modified under a PCCP may not serve a predicate device in its modified form. That is, a firm intending to reference a predicate device with an authorized PCCP cannot reference in its submission versions of the predicate device that contain modifications authorized by the PCCP. The reference must be to the version or configuration of the device originally submitted and approved or cleared without any PCCP-authorized modifications. FDA acknowledges that once the modification is implemented and incorporated into a subsequent 510(k) submission, the device as modified pursuant to the PCCP can serve as a predicate device.[vii]

One significant lesson learned from firms submitting PCCPs, including PCCPs that address AI/ML-enabled device software functions, is not to underestimate the level of effort and detail required to construct a PCCP. It is important that firms clearly think through and thoroughly document the modifications they wish to incorporate into the PCCP, the quality system processes that will be used to support each modification, and how the device will remain safe and effective following each modification. To that end, FDA encourages firms to take advantage of the Q-Submission Program to discuss proposed PCCPs with FDA and gain early feedback that can be incorporated into the submitted PCCP.

IDENTIFYING A PCCP IN A MARKETING SUBMISSION[viii]

The draft guidance indicates that a PCCP should be included as a standalone section within a 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 draft guidance envisions that device labeling will evolve as modifications are implemented. Except for PCCPs focused on manufacturing changes, FDA suggests that labeling likely will need to explicitly describe the authorized PCCP and provide information necessary for a user to understand changes in the device and to continue to use the device safely and effectively as it evolves. The PCCP will also be included in FDA's publicly available device

summaries, such as the PMA summary of safety and effectiveness document (SSED) and approval order, 510(k) summary, or De Novo decision summary. Trade secret and commercial confidential information can be excluded.

UTILIZING AN AUTHORIZED PCCP TO IMPLEMENT DEVICE MODIFICATIONS[ix]

FDA's expectation, of course, is that device modifications will be implemented pursuant to the authorized PCCP. A modification is consistent with the PCCP if it is included in the Description of Modifications in the PCCP and implemented consistent with the Modification Protocol. In such cases, the modification simply needs to be documented within the manufacturer's Quality System.

Again, authorized PCCPs allow modifications of an approved or cleared device to move forward without the need for a subsequent submission. Even so, modifications must still be implemented in compliance with the QSR, specifically the design change requirements under 21 C.F.R. § 820.30(i). The draft guidance does not address FDA's inspectional authority. However, most documents relating to PCCPs will be incorporated in the quality system and it can be expected that FDA's usual inspectional authorities will apply.[x]

If a modification is not described in the PCCP, then the manufacturer would apply the familiar regulatory analysis to determine if it is a change requiring a new marketing authorization.[xi] If the modification is described in the PCCP but not implemented consistent with the Modification Protocol, then FDA is likely to require a new marketing authorization, because a change described in a PCCP by definition would ordinarily require a new marketing authorization, if it were not for the cleared or approved PCCP. The draft guidance "strongly" recommends that manufacturers reaching a different conclusion consult with the appropriate review division.

RECOMMENDED CONTENT FOR A PCCP[xii]

As mentioned above, the draft guidance clearly reflects lessons learned from the experience with AI/ML-enabled software in the past couple of years. One fruit of that experience appears to be a lengthy section describing in detail the kind of content that should be contained in a PCCP submission. It is too long to summarize here, but it bears careful study by anyone who is preparing such a submission. The key takeaway is that, although the manufacturer will not have implemented the proposed planned modifications, such modifications must be developed to the point that they can be well-described, with well-characterized methods for developing and validating the proposed modifications. Additionally, the potential impact on the safety and effectiveness of the device must have been thoroughly considered. FDA has included a series of examples that may be helpful in understanding what is needed in a PCCP submission, and also provides examples of changes that will or will not be appropriate for a PCCP.[xiii]

PROSPECTS FOR SUCCESS OF THE PCCP PATHWAY

The PCCP authority is one of the most promising developments in medical device regulation to come along in many years. If it is successful, it promises to allow industry to innovate more quickly without compromising safety or effectiveness. One unanswered question is the impact on FDA workload. The PCCP pathway could reduce FDA workload by reducing the number of separate applications, though that may be offset by front loading review for modifications that ultimately are not implemented (and thus would never have been the subject of a premarket review).

As to the overall prospects for success, the draft guidance points to a few examples of similar types of planned device evolution.[xiv] For example, FDA allows device expiration labeling to be lengthened without a new review, if done pursuant to the protocol FDA reviewed for the initial expiration date. FDA also allows manufacturers of in vitro diagnostic products to add certain instruments for use with an assay previously cleared for a specific instrument, without requiring a new marketing authorization. But these are fairly simple applications of the concept. Skeptics will point to the Product

Development Protocol (PDP), which is still in the FD&C Act,[xv] as an alternative to PMA approval—but is never used. In the PDP, a manufacturer and FDA essentially must predict and agree in advance to the entire validation program for a Class III device, which is not an easy task. The PCCP pathway is more modest than the PDP pathway because it is focused on specific modifications. Time will tell, but the PCCP pathway could be a game changer.

[i] Specifically, 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 to the FD&C Act.
[ii] Draft Guidance at 6-8.
[iii] *Id.* at 9.
[iv] *Id.* at 9-11.
[v] 21 C.F.R. Part 820.
[vi] Draft Guidance at 11.
[vii] *Id.*
[viii] *Id.* at 11-13.
[ix] *Id.* at 13-15.
[x] As FDA notes, deviations from the authorized PCCP reviewed in the marketing submission would generally cause a device to be adulterated and misbranded under sections 501(f)(1) and 502(o) of the FD&C Act.
[xi] 21 C.F.R. §§ 807.81(a)(3), 814.39(a).
[xii] Draft Guidance at 25-31.
[xiii] *Id.* at 31-37.
[xiv] *Id.* at 2.
[xv] FD&C Act § 515(f).