07 November 2024

Dockets Management Staff (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Rm. 1061
Rockville, MD 20852
via online submission to https://www.regulations.gov/

RE: Docket No.***FDA-2024-D-2338****: FDA draft guidance on Predetermined Change Control Plans for Medical Devices*

Dear Sir or Madam,

The International Society for Pharmaceutical Engineering (ISPE) appreciates the opportunity to comment on the above-referenced draft guidance.

ISPE appreciates the FDA's efforts to illustrate the pathways for device modifications that may be appropriate for inclusion in a PCCP for a 510(k), De Novo, or a PMA device submission. In addition to specific suggestions listed in the attached pages, ISPE requests that FDA consider revising Figure 2 and Figure 3 to more closely align with terminology and language in decision trees depicted in existing FDA guidance documents, such as "Deciding When to Submit a 510(k) for a Change to an Existing Device," (issued 2017, available at: https://www.fda.gov/media/99812/download).

ISPE is a not-for-profit organization of individual members from pharmaceutical companies, contract manufacturing organizations, suppliers and service providers, and health authorities. ISPE's 22,000+ members lead scientific, technical, and regulatory advancement throughout the entire pharmaceutical lifecycle in more than 90 countries around the world. ISPE does not take a political position or engage in lobbying activities or legislative agendas.

We appreciate the opportunity to submit these comments for your consideration. Please do not hesitate to contact me if you have any questions.

Respectfully,

Michael Rutherford
ISPE Interim President and CEO
MRutherford@ispe.org

cc: Jeff Biskup, ISPE Chairman

Response to a request for comments **FDA-2024-D-2338: FDA draft guidance on Predetermined Change Control Plans for Medical Devices**

Comments submitted by the International Society for Pharmaceutical Engineering (ISPE), regulatorycomments@ispe.org

GENERAL COMMENTS ON THE DOCUMENT
We appreciate the FDA's efforts to illustrate the pathways for device modifications that may be appropriate for inclusion in a PCCP for a 510(k), De Novo, or a PMA device submission.

Specific Comments on the Text

ISPE indicates text proposed for deletion with strikethrough and text proposed for addition with **bold and underlining**.

Section or Line Number	Current Text	Proposed Change	Rationale or Comment
124 - 127	• "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"	Add **"Distinguishing Medical Device Recalls from Medical Device Enhancements."**	We recommend including a reference to the FDA guidance document, "Distinguishing Medical Device Recalls from Medical Device Enhancements"(accessible at: https://www.fda.gov/regulatory-information/search-fda-guidance-documents/distinguishing-medical-device-recalls-medical-device-enhancements) as another guidance document that may need to be updated. This guidance is meant to clarify when a change to a device constitutes a medical device recall and distinguishes these changes from device enhancements that do not meet the definition of a medical device recall.

Section or Line Number	Current Text	Proposed Change	Rationale or Comment
300	Reasonable assurance of safety and effectiveness and substantial equivalence of devices with PCCPs	Reasonable assurance of safety and effectiveness and/**or** substantial equivalence of devices with PCCPs	The heading for the general principle should align with the statement on lines 303-304 which distinguishes the substantial equivalence paradigm for certain devices.
336 - 343	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, and as applicable, must allow the device to remain substantially equivalent to the predicate device. 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.	A PCCP should not include a list of any/all modifications that a manufacturer may possibly make. A **PCCP should only consider modifications that a manufacturer may reasonably implement within the existing risk management framework of the device while still ensuring the safety and effectiveness or substantial equivalence of the device.** 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, and as applicable, must allow the device to remain substantially equivalent to the predicate device. If a PCCP includes numerous modifications, or modifications that range across various aspects of the device, **modifications that could introduce new risks 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,** 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.	Having an arbitrary cutoff or limit for the number of modifications that would be considered appropriate for inclusion in a PCCP does not align with the least burdensome principles for premarket review and may significantly limit the utilization and adoption of PCCPs. Section 515C(a)-(c) of the Food and Drug Cosmetic Act, which establishes the regulatory framework for PCCPs for devices, does not specify a numerical limit for the number of changes that can be included in a PCCP. The authorization of a PCCP as part of a device marketing authorization should be based on risk and an assessment that there is a reasonable assurance of the safety and effectiveness, or substantial equivalence of the device based on established controls through the device's risk management framework and manufacturer's quality management system.

Section or Line Number	Current Text	Proposed Change	Rationale or Comment
510-511	When utilizing an authorized PCCP to implement device modifications, the manufacturer should update the labeling for the device as specified in the authorized PCCP.	**If the modification implemented consistent with the authorized PCCP necessitates an update to the labeling**, the manufacturer should update the labeling for the device as specified in the authorized PCCP.	The guidance should more clearly state that the manufacturer should update the labeling for the device if the modification necessitates an update to the labeling per the authorized PCCP because not all modifications may require labeling updates.
766	Modifications that generally **may be appropriate** for inclusion in a PCCP:	ISPE recommends adding the following bullet: • **Certain changes in software to enhance cybersecurity to address a potential vulnerability as part of a device's cybersecurity management plan.**	Certain software changes made to enhance a device's cybersecurity throughout its total product lifecycle should generally be listed as an example modification appropriate for inclusion in a PCCP.
910	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.	To ensure an efficient review, FDA recommends that a PCCP include only **modifications that a manufacturer may reasonably implement within the existing risk management framework of the device while still ensuring the safety and effectiveness or substantial equivalence of the device**	Please refer to previous comments pertaining to lines 335-343 regarding concerns with limiting the number of modifications or having an arbitrary cutoff for the number of modifications that can be included in a PCCP.
Figure 2 & Figure 3		Please consider revising Figure 2 and Figure 3 to more closely align with terminology and language in decision trees depicted in existing FDA guidance documents, such as FDA guidance, "Deciding When to Submit a 510(k) for a Change to an Existing Device," (issued 2017, available at: https://www.fda.gov/media/99812/download). Also, to improve the clarity of the flowcharts,	The flowcharts depicted in Figure 2 and Figure 3 on pages 21 and 24, respectively, are difficult to understand as currently illustrated and creates additional confusion. For example, as depicted, it is unclear why certain modifications are generally not appropriate for inclusion in a PCCP as this could be due to different reasons based on a risk determination, reporting obligations,

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		we recommend including explanatory notes (e.g. footnotes, side notes) and distinguishing paths for different scenarios which clearly illustrate and explain why certain modifications are generally not appropriate for inclusion in a PCCP considering risk determination, reporting obligations, and premarket review requirements etc.	and premarket review requirements. Additionally, the flowcharts do not illustrate instances where certain device modifications may not be appropriate for inclusion in a PCCP because these modifications fall under the documentation requirements as part of a manufacturer's quality management system and would not normally require premarket review.

End of comments