



FDA-2004-N-0191

VIA ELECTRONIC SUBMISSION

June 27, 2018

Dockets Management Staff (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Rm. 1061
Rockville, MD 20852

Re: Docket No. FDA-2004-N-0191: Product Jurisdiction – Proposed Rule

Dear Sir or Madam:

The Combination Products Coalition (“CPC”)¹ welcomes the opportunity to provide comments on FDA’s proposed update to the Product Jurisdiction Rule, 21 CFR part 3.

Overall, the CPC appreciates the FDA’s stated goals of clarifying the rule, aligning the rule with current statutory language, improving the efficiency of the Request for Designation (“RFD”) process, and emphasizing the flexibility and speed afforded by informal processes that are available to sponsors (i.e., the pre-RFD process). However, as highlighted below, significant issues remain in this area, including some that are created by this most recent FDA proposal. Such issues continue to create burdensome ambiguity in classifying a product as a drug, device, or biologic, and determining whether the product is considered a combination product. We hope that FDA will consider our comments as it works to finalize the rule.

I. Removal of Reference to Intercenter Agreements from Section 3.5

The most concerning change for our membership is the Agency’s proposal to remove the discussion regarding the relationship between 21 CFR part 3 and the intercenter agreements from Section 3.5, as these agreements contain substantive information regarding product jurisdiction. We acknowledge that these agreements are outdated and that their usefulness is limited given their age, but the inclusion of specific product classification examples and reasoning behind said classification is critical to understanding future jurisdictional questions. We fully support enhancing transparency and clear articulation of the principles upon which jurisdictional

¹ The CPC is a group of leading drug, biological product, and medical device manufacturers with substantial experience and interest in combination product issues. One of our top priorities is to work collaboratively with FDA on issues affecting combination products to advance our common mission: providing the best possible health care to patients. Our diverse, cross-industry membership permits the CPC to bring a special, broad and unique perspective to these issues.

determinations are based, and prefer that such information be included in this regulation in addition to any current² and potential future guidance.

In addition to jurisdictional clarity, we would also appreciate clarification of considerations for determining when a given product is a combination product, specifically for cross-labeled combination products and products that provide dosing recommendations on the basis of digital health technology (e.g., wearables that monitor physiological parameters or products that track dosing compliance). Again, we prefer that such considerations be included in the regulation, although we understand that a full discussion and examples may be more suited for guidance.

II. Language Concerning Number of Applications for a Combination Product

We are also concerned with the Agency's proposal to remove language from the rule concerning the number of applications to be submitted for the premarket review of combination products. We acknowledge that the 21st Century Cures Act³ amended the Federal Food, Drug, and Cosmetic Act ("FDCA") on this point, but believe that the current implementing language is appropriate for this portion of the regulation, particularly as it relates to how FDA may determine that a single application is necessary for a given combination product, or that separate applications are recommended for constituent parts. We believe that regulatory flexibility that allows a sponsor to file more than one marketing application, when appropriate, is needed.

III. Clarification that 21 CFR Part 3 Applies to Sponsors Only

Regarding the proposal to clarify that 21 CFR part 3 applies to sponsors only (in Section 3.3), while we understand the Agency's reasoning, we would prefer that the rule not preclude others (including trade associations, such as CPC) from formally engaging with FDA on jurisdictional and combination product concerns. We believe that the formal process described in this regulation⁴ that results in a binding decision and transparency is beneficial for industry and allows groups beyond sponsors to utilize these aspects. Such potential engagements would likely include a group of sponsors with similar or aligned jurisdictional concerns or questions that would like to obtain a formal decision on actual situations that require clarity.

On a related note, we understand the value of an informal engagement process (i.e., the pre-RFD process)⁵ and appreciate the ability to use such means to discuss jurisdictional issues with FDA, but we believe the best way of preserving due process and transparency is through the RFD process. As such, we would like to ensure that this remains a viable pathway for all interested parties. Further comment on the RFD process is included later in this document.

² FDA, Classification of Products as Drugs and Devices and Additional Product Classification Issues: Guidance for Industry and FDA Staff (2017), <https://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM258957.pdf>.

³ 21 U.S.C. § 353(g)(6).

⁴ 21 C.F.R. § 3.7.

⁵ FDA, How to Prepare a Pre-Request for Designation (Pre-RFD): Guidance for Industry (2018), <https://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM534898.pdf>.

IV. Clarification Regarding Intercenter Consultations

We understand the proposed clarification of the wording regarding intercenter consultation and coordination in Section 3.4, though we would like to emphasize the importance of this process, which is a key component of the Combination Product Annual Report required by statute.⁶ In addition, we very much appreciate the recent revision of the FDA Staff Manual Guide covering the Intercenter Consult Request Process⁷ in response to an earlier CPC study⁸ that recommended updates to this process. We believe that continued improvements to the review of combination products are in the best interest of all stakeholders, including industry, FDA, and, most importantly, patients.

V. Removal of Reconsideration of Jurisdictional Decisions

Regarding the Agency's proposal to remove the process for reconsideration of jurisdictional decisions described in Section 3.8(c), we ask that FDA ensure that a mechanism is included in the RFD process to ensure that all evidence is fully considered and that appeal processes remain available.

We also recommend that Section 3.5 include a clarification that other information beyond what is specifically included in the RFD will be considered in the decision, including content from any pre-submission engagement as well as publicly available information, which is alluded to in the discussion of the proposed rule.

Finally, we recommend that the page limit for an RFD (15 pages, included in Sections 3.5(a) and 3.7(b)) be increased in order to accommodate the "substantive rationale...that references scientific evidence provided by the sponsor" as well as results from any studies agreed upon by FDA and the sponsor, as discussed in the statute. We recognize the need to balance the length of this document with the time required to issue the determination in the regulation, though we believe an increased page limit would be more in alignment with the pre-RFD approach as well as the information required to substantiate the RFD in the statute.

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⁶ 21 U.S.C. § 353(g)(8)(G).

⁷ FDA, Staff Manual Guide Volume IV – Agency Program Directives, Combination Products, Inter-Center Consult Request Process (2018), <https://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/StaffManualGuides/UCM283569.pdf>.

⁸ CPC, Improving Patient Care through Better Combination Product Regulation: Recommendations to FDA Centers from the Combination Product Coalition (2014), <http://combinationproducts.com/wp-content/uploads/2014/07/May-23-2014-CPC-Paper-Improving-Patient-Care.pdf>.

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Overall, as stated previously, we appreciate the intent of the Agency's proposed updates here, but would like to ensure that our concerns are addressed as FDA finalizes this rule and considers future rulemaking. We appreciate the opportunity to provide input on this proposed rule and are happy to provide additional detail or clarity on any of our comments or recommendations.

Very truly yours,

A handwritten signature in black ink, appearing to read "Bradley Merrill Thompson". The signature is fluid and cursive, with a long horizontal flourish extending to the right.

Bradley Merrill Thompson
On behalf of the Combination Products Coalition