Combination Products Coalition

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July 1, 2013 DRAFT

VIA ELECTRONIC SUBMISSION

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

Re: Docket No. FDA-2013-D-0350: Use of International Standard ISO-10993, "Biological Evaluation of Medical Devices Part 1: Evaluation and Testing"; Draft Guidance for Industry and Food and Drug Administration Staff.

Dear Sir or Madam:

The Combination Products Coalition ("CPC") is pleased to offer its comments on the Draft Guidance for Industry and FDA Staff: Use of International Standard ISO-10993, "Biological Evaluation of Medical Devices Part 1: Evaluation and Testing" ("Draft Guidance").

By way of background, the CPC is a diverse group of drug, biological product, and medical device manufacturers with substantial experience in the combination products area. Our members range in size from small start-ups to multi-billion dollar manufacturers. These companies all share an intense interest in policy issues affecting combination products. Because of our diverse, cross-industry membership, we think the CPC brings a broad and unique perspective to issues affecting combination products.

One of our principal goals is to work with FDA on such issues in order to advance our common mission of providing the best possible health care for patients. In this regard, the CPC has had frequent dialogue with the Office of Combination Products on regulations, guidance documents, and other policy issues that affect combination products and how best to serve patient needs with respect to such products. For example, we have submitted dozens of written comments, policy documents, proposed guidance documents, and other materials to the agency on these issues for nearly a decade. If you are interested, you can find several of these materials on our website: http://www.combinationproducts.com/.

Below we offer our comments on the Draft Guidance. As the CPC's principal goal is to address issues specific to combination products, our comments are not designed to address the specific issues raised by Draft Guidance. Instead, the CPC's comments focus on the need for clarification on the applicability of the Draft Guidance to Combination Products. Specifically, we seek clarification on how sponsors of combination products with device primary modes of

action should apply the principles set forth in the Draft Guidance and the applicability of the Draft Guidance to combination products with a drug or biologic primary mode of action.

I. FDA should provide additional guidance regarding how the principles in the Draft Guidance can be applied to combination products

We appreciate that CDRH stated that the general principles set forth in the Draft Guidance would apply to combination products, but sponsors will require further guidance concerning the additional or modified testing that CDRH says may be required for combination products. In order for sponsors to understand the extent to which additional or modified testing may be required, the Draft Guidance instructs the sponsor to contact the appropriate review division. However, we believe the de facto requirement that sponsors enter into a discussion with the Agency for every product falling under the Draft Guidance creates an unnecessary burden on the Agency and on sponsors. But, most importantly, it creates a burden on patients themselves who will be deprived of timely access to safe and effective combination products.

We recognize the variety and inherent complexity of combination products makes it difficult to draft guidance that can apply to all combination products and that FDA cannot address every nuance of how ISO-10993 will apply to combination products. However, this should not prevent FDA from articulating some general principles on the application of the guidance to combination products. By not including at least some general principles, the number of sponsors that feel compelled to contact FDA on this issue is likely to be significant. . Thus, while it may be easier not providing any general principles on how to apply ISO-10993 to combination products, this is likely to cause FDA to answer the same or similar questions multiple times for different sponsors. This is not efficient for either the Agency or the sponsors.

Instead, FDA should provide a framework sponsors could use to evaluate the need for additional/modified testing and the type of testing that FDA will likely require. This allows the initial analysis of the need for additional/modified testing to be performed by the product's sponsor, which is in the best position to perform this analysis because of its intimate knowledge of the product. Additionally, providing such a framework will reduce the effort and resources required by FDA to address these issues.

We request that FDA incorporate into this guidance document a framework that establishes the additional considerations that sponsors of combination products should analyze to determine the proper biocompatibility testing required to support a combination product's marketing submission.

II. FDA should clarify the applicability of the Draft Guidance to combination products with drug or biologic primary modes of action.

Because the Draft Guidance was issued solely by CDRH, it is unclear whether sponsors should rely on it when evaluating biocompatibility of device constituent parts of combination products with drug or biologic primary modes of action. The issues contained in the Draft Guidance are likely to affect combination products over which CDER or CBER may have jurisdiction. However, it is not apparent that CDRH sought input from the other centers to ensure the consistent analysis of this issue across centers. Such consistency is important,

especially because a standalone device may be subject to the jurisdiction of CDRH whereas a similar device is subject to the jurisdiction of CBER or CDER's because it is incorporated into a combination product.[1]

In general, the principles for evaluating the biocompatibility of a standalone syringe should not differ significantly from the evaluation of a pre-filled syringe. This is not to say that the extent and type of biocompatibility testing will not vary between these two products, as there will be an obvious need to evaluate impact on biocompatibility caused by the interaction between the drug product and the syringe While the other centers may generally defer to the standards established by CDRH for the evaluation of biocompatibility of device constituent parts, this is not always the case. For example, on at least one occasion a CDER review division offered a CPC member company the choice of performing biocompatibility testing on the device constituent part or simply submitting copies of material safety data sheets ("MSDS") for all the materials used in the device constituent part of the combination product.

Therefore, we request that the final guidance document clearly state that the principles set forth therein apply to all device constituent parts of combination products, regardless of the combination product's primary mode of action.

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Kindest Regards,

Bradley Merrill Thompson,
On behalf of the Combination Products Coalition

[1] For example, if a manufacturer sells an injector system on its own and also sells a very similar injector system that is prefilled with a drug or biologic, CDRH will likely have jurisdiction over the stand alone injector system and CDER or CBER would likely have jurisdiction over the prefilled injector system.