



April 9, 2019

VIA ELECTRONIC SUBMISSION

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

Re: Docket No. FDA-2018-D-4417: Center for Drug Evaluation and Research's Program for the Recognition of Voluntary Consensus Standards Related to Pharmaceutical Quality; Draft Guidance for Industry

To Whom It May Concern:

The Combination Products Coalition ("CPC")¹ welcomes the opportunity to provide comments on FDA's draft guidance entitled "CDER's Program for the Recognition of Voluntary Consensus Standards Related to Pharmaceutical Quality"² (the "Draft Guidance").

CPC member companies recognize the usefulness of a well-structured consensus standards program, primarily due to our use of CDRH's Standards and Conformity Assessment Program³ (the "CDRH Program") for the device constituent parts of our various combination products marketed in the United States. The CDRH Program affords industry the opportunity to participate along with regulatory authorities, such as FDA, in the bodies that create and maintain such consensus standards. Additionally, these standards play a significant role in promoting international harmonization in the regulation of medical products, which is of interest to both industry and regulatory authorities. For these key reasons, we support the implementation of a similar voluntary consensus standards program within CDER, as proposed by the Draft Guidance (the "CDER Program").

However, as the Draft Guidance is relatively broad, covering "voluntary consensus standards related to pharmaceutical quality for products under CDER's jurisdiction," CPC would

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.

² <https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM631269.pdf>.

³ <https://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/Standards/default.htm>.

like to provide certain input to the Agency, as detailed below, from the standpoint of manufacturers of combination products under CDER jurisdiction (e.g., drug/biologic Primary Mode of Action) with device constituents. We hope this feedback will be helpful to the Agency during the formative stages of this new CDER Program.

First, we ask that FDA confirm that the scope of this Draft Guidance includes combination products under CDER jurisdiction. As stated above, CPC sees value in the implementation of such a program and would like to see such products explicitly fall within the scope of the CDER Program. We also request that FDA confirm which elements of the combination product fall within the scope of the CDER Program, such as design and manufacture, including applicability to the device constituent part(s).

Second, we ask that FDA clarify how this proposed CDER Program will align with the aforementioned CDRH Standards and Conformity Assessment Program for the device constituent(s) of combination products under CDER jurisdiction. Currently, the applicability of the CDRH Program to such products is not explicitly clear; although such device constituents are not directly within the scope of CDRH's Program, recognized device consensus standards are generally applied to device constituents as taken from similar non-combination device product codes. In addition, CDRH provides staff members to participate in the development of standards that apply to the device constituent of combination products (e.g., ISO 11608). CPC supports such an approach; in fact, many member companies have taken the opportunity to participate in bodies covering applicable standards, and the application of these standards has allowed for consistency and clarity in combination product submissions and reviews.

To ensure transparency, CPC requests that FDA explicitly state in the Draft Guidance that the CDER Program applies to the device constituents of combination products under CDER jurisdiction to ensure the continuation of such an approach. Additionally, we support specifically applying the existing CDRH Program to device constituents of such products, as that program is well-established and, as mentioned above, has already been effectively used for such products for some time. If this approach is taken, we also recommend clarifying which elements of the existing CDRH Program⁴ may be applied to the device constituent (e.g., General Use of Consensus Standards, or Declarations of Conformity – which have generally not been used for combination products under CDER jurisdiction). As with other elements of combination product regulation (e.g., current Good Manufacturing Practices⁵ and Postmarket Safety Reporting for Combination Products⁶), we appreciate FDA's efforts to create consistency while also streamlining requirements for combination products and avoiding unnecessary duplication. We believe that a well-crafted program here could clarify the approach for CDER-led combination products while also utilizing the existing CDRH standards program.

⁴ FDA, *Appropriate Use of Voluntary Consensus Standards in Premarket Submissions for Medical Devices: Guidance for Industry and FDA Staff* (2018), <https://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm077295.pdf>.

⁵ 21 C.F.R. § 4, Subpart A.

⁶ 21 C.F.R. § 4, Subpart B.

Third, we request that FDA clarify how the informal nature of the CDER Program will ensure predictability and consistency across CDER for the same device constituent and the same standard. We note that the Draft Guidance repeatedly emphasizes the informal nature of the CDER Program. For example, in Section VI.A., the Draft Guidance states, “As stated earlier in this draft guidance, even if an applicant decides to use one of CDER’s informally recognized voluntary standards, CDER may request that the applicant provide additional information to support an IND application or a marketing application.” In order for such a recognition program to provide a meaningful benefit to both industry and FDA, both parties have to understand how FDA will respond to a development program that a sponsor has followed in good faith based upon a standard recognized by FDA.

The Draft Guidance states that the CDER Program is different from the CDRH Program, but fundamentally the description of the program is very similar to the CDRH Program without the commitment to honor the recognized portions of the standard. The CDRH Program does afford flexibility to the review staff to request additional information not covered by the recognized portions of the standard, but the expectation is that this additional information would only be requested regarding information not covered by the standard. This is a key commitment for success of the program. Therefore, CPC requests that CDER also offer the same good faith commitment to honor the requirements of the recognized portions of a standard.

Finally, we ask that FDA clarify the type of standards that are expected to be a part of the CDER Program, i.e., whether it is intended to cover specific and/or targeted standards (such as ISO 11608-1 *Needle-based injection systems for medical use – Requirements and Test Methods, Part 1: Needle-based injection systems*), and/or vertical standards that cover wider areas, including portions of the Quality Management System (such as ISO 14971 *Medical devices – Application of risk management to medical devices*).⁷ The CDRH Program includes such vertical standards, which CPC finds to be beneficial, allowing manufacturers to utilize consensus-driven approaches across the organization in order to meet cGMP as well as individual product requirements.

We appreciate the opportunity to provide input on this Draft Guidance and look forward to further dialogue with the Agency to clarify or discuss any of our suggestions.

Very truly yours,



Bradley Merrill Thompson,
On behalf of the Combination Products Coalition

⁷ Note that both examples (ISO 11608-1 and ISO 14971) are CDRH-recognized consensus standards commonly applied to device constituents of combination products under CDER jurisdiction, such as pre-filled injectors.