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21 July 2021

Policy Bureau
Health Products and Food Branch
Health Canada
Ottawa, Ontario K1A 0K9
Canada

Re: Issue Identification Paper: Drug-Device Combination Products (DDCPs) Draft for Consultation

Dear Madam or Sir:

PDA appreciates the opportunity to comment on Health Canada's draft *Issue Identification Paper: Drug-Device Combination Products* (DDCPs). PDA applauds the issuance of this issue identification paper as a first step in exploring the topics that could benefit from additional regulatory clarity. We strongly support the goal of developing policies and guidance that are easily understood by agency staff and regulated industry alike.

In the attached comment table, PDA offers suggested considerations as Health Canada takes its next steps toward providing more detail and clarity on the classification and regulation of DDCPs. At this time, we seek to assist only by identifying additional questions that may arise under the current policy. We look forward to further engagement as Health Canada works to find solutions to the identified topics.

As Health Canada gathers information to inform future policy development, we encourage you to review the approaches used by other global regulatory authorities. Several other leading regulators have recently reviewed or revised their regulation of DDCPs. Health Canada might be able to build on learnings from those activities. Moreover, alignment among global regulators, wherever possible, can simplify dialogue with industry, improve industry understanding of expectations, and facilitate the introduction of new products and product improvements to benefit Canadian patients.

PDA is a non-profit international professional association of more than 10,000 individual member scientists having an interest in the fields of pharmaceutical, biological, and device manufacturing and quality. Our comments have been prepared by a committee of global experts in combination products on behalf of PDA's Biopharmaceutical Advisory Board and Board of Directors.

If you have any questions, please do not hesitate to contact me via email at johnson@pda.org.

Sincerely,

Richard Johnson
President and CEO

cc: Glenn Wright, PDA; Josh Eaton, PDA

Health Canada
Draft Issue Identification Paper: Drug-Device Combination Products
12 July 2021

General Comments

Section	General Comments	Rationale
General	As Health Canada further develops and clarifies its policies, PDA strongly recommends that Health Canada carefully consider the approaches used by other global regulatory authorities for both learnings and opportunities for alignment.	Several other regulatory authorities, including the US Food and Drug Administration (FDA) and the European Medicines Agency, have given significant thought to the regulation of drug-device combination products in recent years. While their legal frameworks for these combination products may differ slightly from Canada's, key elements are standard. Further, with of the global nature of pharmaceutical and medical device manufacturing, alignment between regulators can help these products reach patients in Canada efficiently.
1	PDA encourages Health Canada to develop and describe a clear mechanism through which manufacturers can ask the agency for a determination or adjudication of a product's combination product classification. For instance, US FDA describes procedures for obtaining regulatory feedback on combination products in guidance documents, including "Requesting FDA Feedback on Combination Products," available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/requesting-fda-feedback-combination-products and "How to Write a Request for Designation (RFD)," available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/how-write-request-designation-rfd	To efficiently bring products to Canadian patients, it is helpful for manufacturers to be able to consult Health Canada on key questions, including: • Is my product a drug-device combination product? • Will my product be subject to the Food and Drug Regulations or the Medical Device Regulations? The answers to these two questions will not be obvious for many products. Early communication and information-sharing can help the manufacturer and the agency understand key points. A clear procedure, along with definition of the information that would be useful to Health Canada, can facilitate these conversations and improve regulatory outcomes.
3.1	It would be very helpful to industry if Health Canada would identify the specific testing and standards of evidence that apply for drug delivery systems. Similarly, clarifying the aspects of ISO 11608 that apply would help manufacturers understand the agency's expectations for both regulatory filings and compliance.	It would be ideal for regulated industry and Health Canada to share a clear understanding of the testing requirements and ideal timing for conducting such testing during product development. This would benefit industry compliance and also should assist in regulatory review and approval.

Section	General Comments	Rationale
3.3	PDA feels that there is much to be clarified regarding the application of GMPs to different types of products. The language in this section relating to "packaging requirements under GMPs" is especially confusing. It would be helpful if Health Canada were to specify exactly the elements of ISO 13485 that apply. Health Canada also might address clearly the GMP requirements for single-entity drug-delivery systems.	The agency's review staff as well as industry may benefit from shared understanding of the specific requirements to ensure GMP compliance and standard conformity.
3.4	While Health Canada includes considerations for post-marketing reporting, PDA suggests that Health Canada also include discussion of general principles for product lifecycle management for combination products based on principles developed in ICH Q12 "Technical and Regulatory Considerations for Pharmaceutical Product Lifecycle Management."	Combination products are within the scope of ICH Q12, and issues relating to lifecycle management certainly are arising and will continue to arise. While Canada may not yet have formally adopted ICH Q12, PDA strongly encourages Health Canada to use the principles in that guidance document as a basis for any information and policies.

Specific Comments to the Text

Line No.	Current Text	Proposed Change	Rationale
Section 1.2 - Products not classified as DDCPs	**Kits** A kit consists of two or more health products that are contained in one package for convenience purposes but are not required to be combined prior to administration or use. The products are often separately licensed. As such, the Policy does not apply.	**Kits** Two or more ***licensed*** health products that are *provided to the use*r in one package that are intended to be used together in a manner consistent with the indication and/or use for which they are licensed. As such, the Policy does not apply.	The definition/description is not consistent with definitions in other regions of the world and is confusing. In particular, PDA recommends omitting terms such as "combined" and "convenience" because they are not defined and have multiple possible interpretations. The proposed text more clearly characterizes the products that are excluded from classification as DDCPs and is consistent with this paper's

Line No.	Current Text	Proposed Change	Rationale
			focus on product approvals. The revised text also is consistent with the other examples of kits that contain drugs and devices that are provided in Health Canada documents.
	Cross-labelled products With cross-labelled products, the drug and device components are individually authorized and sold separately but are labelled to be used together exclusively. The respective labelling for each product cross-references the other product(s) for either concurrent or successive administration. Since these products are not integrated in a singular entity, the Policy does not apply.	**Combined Use products** With *Combined Use products,* the drug and device components are individually authorized and *packaged/distributed separately, where the products as provided in their labeling are intended to be used together to achieve the intended use, indication or effect.* Since these products are not integrated in a singular entity, the Policy does not apply.	The important issue with these products is that they are individually authorized and packaged/distributed separately, are n*ot* integrated in a singular entity, and are in some way intended to be used together. The exclusivity and nature of the labeling (one-way or cross-labeled) is not important to this policy.