Comments and suggestions from reviewer

Title: WHO Global Model Regulatory Framework for medical devices including in vitro diagnostic medical devices. (GMRF) (replacing the 2017 version published as Annex 4 in the WHO Technical Report Series 1003). **(WHO/BS/2022.2425)**

Reviewer's Name (first name/last name): Submitted on behalf the below
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Sections/page and line No.	Original Text	Comment	Suggested Amendment	Internal Use Only [blank]
GENERAL COMMENT				
ISPE recognizes and thanks the WHO for taking into consideration ISPE's comments made in responses to the Global Model Regulatory Framework for medical devices including 4 IVDs (GMRF) Draft 2, May 2022. ISPE does have one important comment regarding borderline products, below.				
Introduction and objectives				
Definition, classification, essential principles, and conformity assessment of medical devices				

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Enabling conditions for effective regulation of medical devices including IVDs				
Establishing a stepwise approach to regulating medical devices				
Regulatory pathways				
Section 5, page 94, footnote 40	[40] Borderline products are generally (medical) products that offer combined characteristics that are covered by at least two legislations (e.g., both medical device and medicinal product), whose lead legislation within a jurisdiction may be unclear Borderline products are not combination products. Please see Section 5.6.	Combination products are medical products that have two or more differently regulated medical products (constituent parts), such as a medicinal product and a medical device. This overlaps with the definition of "borderline products." With that, while not all borderline products are necessarily combination products, some might be. The concept of Primary Mode of Action is commonly applied across jurisdictions to aid in determining the lead legislation (for example,	[40] Borderline products are generally (medical) products that offer combined characteristics that are covered by at least two legislations (e.g., both medical device and medicinal product), whose lead legislation within a jurisdiction may be unclear. ~~Borderline products are not combination products~~ **In the combined use context, however, some borderline products might be considered combination products.** Please see Section 5.5.	

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		device or medicinal product) to apply to medical products. Whether formally classified as medical devices, medicinal products (drugs, biological products), or combination products, ensuring product safety and efficacy necessitates application of appropriate, cross-cutting expertise in development, review, and throughout the product lifecycle with regard to each constituent part and their combined use. In most cases, the distinction between device and drug primary mode of action (PMOA) is clear, and the lead regulatory construct for the combination product can be readily identified. Where PMOA is not clear, it is important for the sponsor to speak to the health authority within a jurisdiction to ensure clarity to avoid missteps and delay.		

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		Additionally, we think the appropriate section to reference is Section 5.5, Regulatory Pathways for Combination Products, rather than Section 5.6, Regulatory Pathways for Donated Products		
Additional topics				
Implementation				
References				
Other comments				