EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

12 May 2017

Submission of comments on "Concept paper on developing a guideline on Quality requirements of medicinal products containing a device component for delivery or use of the medicinal product"
(EMA/CHMP/QWP/BWP/661488/2016)

Comments from:

Name of organisation or individual
International Pharmaceutical Aerosol Consortium on Regulation and Science (IPAC-RS)

IPAC-RS is an association of companies[1] that develop, manufacture and market drug-device combination products for drug delivery to the respiratory tract. As such, IPAC-RS has significant experience with these product types, and welcomes the opportunity to provide feedback on the Concept Paper EMA/CHMP/QWP/BWP/661488/2016. In addition, IPAC-RS would be willing to meet with the Agency to discuss these issues further in an appropriate setting, including a public workshop.

[1] IPAC-RS Member Companies are listed at http://ipacrs.org/about/list-of-member-companies/

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1. General comments

Stakeholder number *(To be completed by the Agency)*	General comment (if any)	Outcome (if applicable) *(To be completed by the Agency)*
	IPAC-RS welcomes the Concept Paper and would be willing to work with the Agency, as appropriate, to discuss the points made in these Comments. IPAC-RS recommends that the future guideline: 1. Apply prospectively to new products (not retrospectively to the already-approved products on the market). 2. Be aligned with the new Medical Device Regulations (MDR). a. Of special interest is how this future guideline will handle devices that until recently were not considered devices per the Medical Device Directives (such as certain components of an inhalation delivery system) but may be viewed as devices per the new MDR. 3. Discuss different device classes that might be used in a drug-device combination (DDC) product, with examples. a. Include in the consideration various digital components and e-connected products. b. Explicitly include add-on devices, such as spacers and holding chambers, which are commonly (albeit	

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	not always) used for delivery of medicines from pressurized metered dose inhalers (pMDIs). Such inclusion would help ensure consistency of requirements and assessments. 4. Establish a clear definition for DDC products so that all interested parties, including industry and regulators, understand where the boundaries between different product types lie. Sub-categories of DDC products should also be taken into account where appropriate. Ideally, this guideline would address all classes of DDC products. 5. Be aligned with existing European guidelines, e.g., for orally inhaled products (OIPs), which is a type of DDC products. 6. Be aligned with existing international consensus standards (e.g., from ISO), especially with regard to definitions, terminology, and risk-based approaches. ISO has a number of standards for drug delivery systems and devices that may be used as part of a DDC. 7. To the extent possible, be harmonized with the numerous US FDA guidances for DDC products (incl. OIPs), and with the US Quality Systems regulations, since global companies have to comply with every region's requirements.	

2. Specific comments on text

Line number(s) of the relevant text *(e.g. Lines 20-23)*	Stakeholder number *(To be completed by the Agency)*	Comment and rationale; proposed changes *(If changes to the wording are suggested, they should be highlighted using 'track changes')*	Outcome *(To be completed by the Agency)*
47-50		Comment: The sentence states "*for CE marked medical devices provided separately but sometimes co-packaged….Notified Body may not fully take into account the characteristics of the specific medicinal product that the device is to be used with*". This sentence is contrary to the Essential requirements Checklist that specifically states that medical devices should be tested with the intended medicinal products. Examples should be provided for cases where there are exceptions from either the Medicinal Products Directive or Medical Devices Directive. Proposed change: Please provide examples. Also stress that Notified Bodies and Competent Authorities should work closer together to ensure that the two components of a DDC (device and medicinal product) are not considered as two separate entities but as two components forming a DDC product.	
54-58		Comment: Re the statement: "*In contrast, in situations where the device and the medicinal product form a single integral product which is intended exclusively for use in the given combination and which is not reusable, the medical device is not assessed by a Notified Body and assessment of all of the above aspects, including compliance with Annex 1 to the MDD, is conducted as part of the assessment of the application for marketing authorisation.*"	

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		This statement is appropriate, but it needs to be implemented in practice more consistently. Some of the IPAC-RS member companies encountered the opposite advice; e.g., when seeking scientific advice at the pan-EU level relating to a DDC, the verbal response from regulators indicated a requirement of a CE mark and an NB assessment prior to submission of the MAA for the DDC. Proposed change: Notified Bodies and Competent Authorities need to have clear mechanisms for aligning their interpretation and implementation of the guideline.	
57-58		Comment: Re the statement: "…*compliance with Annex 1 to the MDD, is conducted as part of the assessment of the application for marketing authorisation*". Typical assessment is done in terms of compatibility and clinical performance. Ideally, this should be mandated for all applications and made a requirement. Proposed change: Clearly state that such assessment is required for all DDC applications.	
76-78		Comment: Re the statement "*The guidance will not specifically address issues related to integral device as part of combined advanced therapy medicinal products (cATMPs as per Regulation (EC) No 1394/2007) but it is expected that the same principles*	

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		will apply." The latter part of the statement ("*but it is expected that the same principles will apply*") could be misread as ambiguous and open to interpretation. The preference is always clarity on whether principles apply. <u>Proposed change</u>: Consider a more clear statement, to avoid potentially diverging interpretations by the Notified Bodies, Competent Authorities, and industry.	

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