2 November 2023

European Commission, Directorate-General for Health and Food Safety

Reference: CELEX number: 52023PC0192
Proposal for a DIRECTIVE OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL on the Union code relating to medicinal products for human use, and repealing Directive 2001/83/EC and Directive 2009/35/EC
COM/2023/192 final

Dear Sir or Madam,

The International Society for Pharmaceutical Engineering (ISPE) appreciates the opportunity to comment on the above-referenced **Directive.**

ISPE has significant comments related to distributed manufacturing in support of companies which may have or propose to have decentralised manufacturing facilities in several EU member states as well as other locations throughout the world.

ISPE is a not-for-profit organization of individual members from pharmaceutical companies, contract manufacturing organizations, suppliers and service providers, and health authorities. The 21,000+ members of ISPE lead scientific, technical, and regulatory advancement throughout the entire pharmaceutical lifecycle in more than 90 countries around the world. ISPE does not take a political position or engage in lobbying activities or legislative agendas.

Specific comments on the articles are attached.

ISPE appreciates the opportunity to submit these comments for your consideration. Please do not hesitate to contact me if you have any questions.

Respectfully,

Thomas B. Hartman
ISPE President and CEO
thartman@ispe.org

cc: Scott Billman, ISPE Board Chair

Response to a request for comments EUC Document 52023PC0192 Proposal for a

DIRECTIVE OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL
on the Union code relating to medicinal products for human use, and repealing Directive 2001/83/EC and Directive 2009/35/EC

Comments submitted by the International Society for Pharmaceutical Engineering (ISPE), regulatorycomments@ispe.org

Specific Comments on the Text

ISPE indicates text proposed for deletion with ~~strikethrough~~ and text proposed for addition with **bold and underlining**.

Section or Line Number	Current Text	Proposed Change	Rationale or Comment
Article 148.5	For the purpose of paragraph 2 the manufacturing authorisation holder of the central site shall submit a registration form that shall include, at least, the following information: (a) name or corporate name and permanent address of the decentralised site and a proof of establishment in the Union; (b) the medicinal products that are subject to manufacturing or testing steps in the decentralised site, including the manufacturing or testing activities to be performed for those medicinal products; (c) particulars regarding the premises of the decentralised site and the technical equipment to carry out the relevant activities; (d) the reference to the manufacturing authorisation of the central site; (e) the written confirmation referred to in Article 144(2), second subparagraph,	The text within Chapter XI, Article 148 appears to limit decentralised manufacture to within the bounds of the EU. It is suggested to update the line as follows "…the MAH of the central site shall submit a registration form that shall include, at least, the following information (a) name or corporate name and permanent address of the decentralised site and proof of establishment in the Union, **if the site is located within the Union;"**	Many scenarios may involve decentralised manufacturing between the EU and other countries for example the US (if for example, a product is developed and manufactured in the US, the decentralised site may be replicated for commercialization in the EU). It is critical to not limit decentralised manufacturing to occur only within the EU. In addition, it is recommended to provide an allowance for portable manufacture (such as in a mobile cleanroom). These sites would not have a "permanent address" but there are other means to track real-time location (GPS trackers, updates to an online database, etc.)

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Section or Line Number	Current Text	Proposed Change	Rationale or Comment
	that the manufacturer of the medicinal product has verified compliance of the decentralised site with principles of good manufacturing practice referred to in Article 160 by conducting audits		
Article 153.1b	(b) in the case of medicinal products imported from third countries, irrespective of whether they have been manufactured in the Union that each production batch has undergone in a Member State a full qualitative analysis, a quantitative analysis of at least all the active substances and all the other tests or checks necessary to ensure the quality of the medicinal products in accordance with the requirements of the marketing authorisation.	Art. 153.1b: Proposed additional text: Provision for **waiving of import testing** should be extended to countries following the unilateral reliance approach for inspections by trusted non-EU authorities in Articles 188.4a & 190.1d	Future flexibility is desired related to waiving of import testing.
Article 162 – 3	Distributors who intend to import a medicinal product from another Member State shall notify the marketing authorisation holder and the competent authority of the Member State to which the medicinal product is to be imported of their intention to import that medicinal product.	To prevent drug shortages we suggest including a request that the distributor should alert the company and Member State competent authority from which the product will be exported.	We suggest the information should be shared with both the NCA of the member state to which the product is going and the NCA from the member state from which the product will be transferred. This information sharing may help prevent drug shortage in the member state from the drug being exported.
Article 188 – 3	The competent authority of the Member State shall ensure that the measures referred to in paragraph 1, second subparagraph, are carried out by the official representatives of the competent authority of the Member State:	For decentralised sites, we suggest a requirement for a harmonized procedure for inspection and inspection outcomes between EU and third countries to avoid	ISPE suggests that there is a harmonized way of inspection within the EU and in third countries for decentralised manufacturing sites.

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	(a) at an appropriate frequency based on risk, at the premises or on the activities of manufacturers of medicinal products, located in the Union or in third countries, including where appropriate at central or decentralised site(s), and at the premises or on the activities of wholesale distributors of medicinal products located in the Union; (b) at an appropriate frequency based on risk, at the premises or on the activities of the manufacturers of active substances located in the Union or in third countries and at the premises or on the activities of importers, or distributors of active substances, located in the Union.	creating discrepancies between the various decentralised sites.	
Article 218	**Section Article 218 "**Transitional provisions"	**Dir 218** **Consider adding:** 7. The Commission shall ensure continuation of applicability of the Sectoral Annexes on Pharmaceutical Good Manufacturing Practices (GMPs) in Agreements on Mutual Recognition between the Union and 3rd countries, as established.	We recommend that the following is added to Art. 218 of the Directive to ensure that MRAs are kept operational. We believe that the Commission acts only if the legislation advises to do so. For example, the MRA went out of operations during the Medical Device Regulation (MDR) implementation between EU and Switzerland, which demonstrated that changes in the legislation, even adopted by the MRA partner impacted the EU position.

End of Document.

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