ISPE Regulatory Comment Form

Proposed Regulation/Guidance Document: European Commission Eudralex The Rules Governing Medicinal Products in the European Union, Volume 4, EU Guidelines for Good Manufacturing Practice for Medicinal Products for Human and Veterinary Use, Part 1, Chapter 8: Complaints, Quality Defects and Product Recalls

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General Comments
There are no general comments

	SECTION	COMMENT / RATIONALE	PROPOSED CHANGE (IF ANY)

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	Principle	The addition of certain words (i.e. assess and CAPA) to this paragraph will better reflect the introduction of QRM principles and make the section more effective.	Amend Principle to red: "In order to protect public and animal health, a system and appropriate procedures should be in place to record, assess, investigate and review complaints including potential quality defects, and if necessary, to effectively and promptly recall medicinal products for human or veterinary use and investigational medicinal products from the distribution network. Quality Risk Management principles should be applied to the investigation and assessment of quality defects and to the decision-making process in relation to product recalls, Corrective and Preventative Actions (CAPA) and other risk-reducing actions. Guidance in relation to these principles is provided in Chapter 1."
	8.2	Personnel involved should be trained and an assessment performed.	Amend 8.2 to read: "Sufficient trained personnel and resources should be made available for the handling, assessment investigation and review of complaints and quality defects and for implementing any risk-reducing actions. Sufficient trained personnel and resources should also be available for the management of interactions with competent authorities."

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	8.8 ii	Significance of distribution especially for temperature sensitive products has not been highlighted. (See also comments below which proposes new wording for items iii & iv and in which the reference to distribution in these sections has been deleted.)	Amend 8.8 sub-point ii, second sentence to read: "The checking or testing of reference and/or retention samples should be considered as part of this, and in certain cases, a review of the batch production record and batch distribution record (especially for temperature sensitive products) should be performed."
	8.8 iii & iv	It is to be expected that there will be a time framing for responding to a complaint and close out of a complaint. In this respect the severity of the complaint should be considered when setting this timeline.	Delete reference to distribution information in section iii and Amend 8.8 iii & iv to read: iii.The need to request a sample of the defective product from the complainant and, where a sample is provided, the need for an appropriate evaluation to be carried out. iv The decision making process that is to be used concerning the potential need for risk-reducing actions to be taken in the distribution network, such as batch or product recalls, or other actions. The assessment of the risk(s) posed by the quality defect based upon severity and extent of the quality defect.

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	8.8 v.	Order to highlight the importance of notification to NCA	Amend 8.8 sub-point v to read: "The assessment of the impact that any recall action may have on the availability of the medicinal product to patients/animals in any affected market and the need to notify the relevant authorities of such impact."
	8.15	This section lacks emphasis on QRM principles	Amend 8.15 to read: "8.15 An appropriate level of root cause analysis work should be applied based upon risk during the investigation of quality defects. In cases where the true root cause(s) of the quality defect cannot be determined, consideration should be given to identifying the most likely root cause(s) and to addressing those using a science and risk-based approach."
	8.19	PQRs as a data source has not been included	Amend 8.19 to read: "Quality defect and corrective and preventative action records and product quality reports (PQR) should be reviewed and trend analyses should be performed regularly for any indication of specific or recurring problems requiring attention.

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	8.23	Agents or traders (brokers) involved in the distribution chain have not been included.	Amend 8.23 to read: "The batch/product distribution records should be readily available to the persons responsible for recalls, and should contain sufficient information on wholesalers, distributors or third parties and directly supplied customers (with addresses, phone and/or fax numbers inside and outside working hours, batches and amounts delivered), including those for exported products and medical samples."
	8.29	It is to be expected that a recall will have an official "close out". Recalls should be closed when the desired amount of product is recalled and a decision taken on recalled product is executed.	Amend 8.29 to read: "The progress of the recall process should be recorded until closure and a final report issued. Progress records and the final report should include a reconciliation between the delivered and recovered quantities of the concerned products/batches."