EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Submission of comments on Revised EC guideline on API Good Distribution Practices

2013-02_gdp_for_api_cons.pdf

Comments from:

Name of organisation or individual
EFPIA

Please note that these comments and the identity of the sender will be published unless a specific justified objection is received.

When completed, this form should be sent to the European Medicines Agency electronically, in Word format (not PDF).

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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)*
	EFPIA welcomes the guideline clarifying the requirements for GDPs for Active Substances.	
	It would be helpful to add a definition table, e.g. distribution point, procuring...	
	It should be clarified that this Guideline complement the European requirements and does not replace or supersede ICH-Q7 and EU-GMP Part II. References to these existing standards should be made throughout the text as appropriate.	

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)*
Scope Paragraph 1		Clarify that starting materials and intermediates are out of scope. Clarify that registration only applies to distributors located in Europe.	
Paragraph 1 + 2		Please reference EU GMP Part II, Chapter 17 "Agents, Brokers, Traders, Distributors, Re-packers and Re-labellers"	
Paragraph 5		Proposed change (if any): The size, structure and complexity of distributor's activities as well as the API distributed should be taken into consideration when developing or modifying the quality system.	
Paragraph 6		Please provide clarification on distribution point or if this could be read as distribution organization.	
Paragraph 6		Proposed change : A management representative should be appointed in each distribution organization	
Paragraph 7		Proposed change : Key personnel involved in the distribution (including the warehousing) of active substances should have …	
Paragraph 9		Proposed change: All documentation in scope of this guideline...	
Paragraph 10		Comment: The reference made is incorrect Proposed change : change "2001/83/EU" into "2011/62/EU"	
Paragraph 11		Proposed change: These procedures should be written and reviewed by knowledgeable personnel, then approved, signed and dated by the person responsible for the quality system.	
Paragraph 12		Proposal: They should be retained for a period of at least five years after expiry date of API.	

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		Replace "is taken" with "is conducted"	
Paragraph 13		Proposed change (if any): Suggest revision of first sentence to read: Records should be kept of each purchase and sale, showing the date of purchase or supply, name of the active substance, batch number and quantity received or supplied, the name and address of the original manufacturer, and the name and address of the consignee. And add to the bullet list: • name and address of the consignee Also, remove from the text the items that are listed in the bullets and list all content under the bullets.	
Paragraph 14		Proposed change : Suggest revision of second sentence to read: Monitoring devices…should be calibrated periodically	
Paragraph 15 last line		Proposed change: Deliveries should be examined at receipt in order to check that containers are not damaged, all security seals are present with no evidence of tampering and that the active substance (quantities) and the consignment correspond to the order.	
Paragraph 17		Proposed change (if any): Where the distributor suspects that an active substance procured or imported by him is falsified or was diverted, he should inform the national competent authority in which he is registered.	
Paragraph 18		Comment: There is no GMP requirement to store APIs separately from Excipients for example. This requirement should therefore be limited to non-pharmaceutical material. Proposed change (if any): Active Substances should be normally be stored apart from other non-pharmaceutical goods…	

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Paragraph 18 line 3		Delete the word "periodically".	
Paragraph 18		It is proposed that records of storage are regularly reviewed by the person responsible for the quality system. It is suggested that this responsibility is rephrased to avoid specifying who should conduct this review. *Proposed change:* 'The records should be reviewed regularly.'	
Paragraph 18 & 22		These paragraphs suggest that Active Substances should be physically segregated. The guideline should recognise the increasing use of validated Warehouse Management Systems and the possibility of random storage and electronic segregation. *Proposed change:* Include text clarifying that electronic segregation within a validated system is acceptable.	
Paragraph 22		Comment: Provide an opportunity for the investigation of the active substances prior to disposition. Proposed change (if any): Active substances with broken seals, damaged packaging, or suspected of possible contamination should be investigated, withdrawn from saleable stock, and if not immediately destroyed, they should be kept in a clearly separated area until their final disposal so that they cannot be sold in error or contaminate other goods.	
Paragraph 23		Comment: The sentence needs rephrasing: "Shortages that requires registered importers to notify relevant customers of any interruption to supply that the importer or distributor becomes aware of." Proposed change (if any): Should be moved to: **Deliveries to customers** Suggest revision to read:	

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		Registered importers are required to notify relevant customers of any shortages that will cause any interruption to supply.	
Paragraph 24		Comment: incorrect references and wording Proposed change (if any): Supplies of API within the EU should be made only by registered distributors of active substances according to Article 52a of Directive 2011/62/EU or to authorized manufacturers according to Article 40 of Directive 2001/83/EC.	
Paragraph 25 a)		Comments to be added: The identification should be not only maintained but also protected from modification a) their identification as well as original manufacturer name and address mentioned on container labels are not lost or adulterated,	
Paragraph 26		Comment: add "Where transportation of the active substance is contracted out, the distributor must have quality agreements in operation with the contract acceptors." Justification: it will be very difficult for the manufacturing authorisation holder to fulfil the requirements on GDPs for active substances, if these contract activities are not covered by quality agreements.	
Paragraph 27		Comment: " Active substances requiring controlled temperature storage should also be transported by appropriately specialized means." A differentiation should be made concerning the distribution conditions which might differ from storage conditions for short terms during transportation which must then be based and justified depending on additional stability studies e.g. cycling studies.	

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		Proposed change (if any): " The appropriate temperatures for active substances should be maintained during transportation to ensure the products quality and shelf-life.	
Transfer of Information Paragraph 30 line 3/4		Comment: The text appears to give no flexibility in how the "customer" gets the required CoA for goods received. For example a company may receive an API from a managed supplier. They would receive a CoA and input this into their QMS/LIMS system, then provide a number of internal and/or contractor sites with the same API and a CoA generated from their site QMS (rather than copies of the original supplier CoA). This could be acceptable if the company has QA Agreements with the API supplier and with the sites it supplies, it retains the original CoA, has a Quality system defining the process etc. Proposed change (if any): Modify text to allow the above – can be either a copy of the original or if within a single company and its internal sites/managed contractors this can be via a documented/validated quality system?	
Paragraph 35		"a) the active substance is in the original unopened container(s), and in good condition;" Proposal to add: the active substance is in the original unopened container(s), all security seals are present and in good condition;	
Paragraph 35 b)		Comment: The period to be covered by the control should be indicated Proposed change (if any): it is demonstrated that the active substance have been stored and handled under proper conditions since it left the care of the Distributor;	

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Please add more rows if needed.