Connecting a World of Pharmaceutical Knowledge

29 April 2013

EUROPEAN COMMISSION
Health and Consumers Directorate-General
Unit SANCO/D/6,
DM24 02/050,
BE-1049 Brussels.

Email: sanco-pharmaceuticalsd6@ec.europa.eu

Subject: Submission of comments for Guidelines on the Principles of Good Distribution Practices for Active Substances for Medicinal Products for Human Use
(Ref. Ares(2013)148102-05/02/2013)

Dear Sir/Madam:

Thank you for the opportunity to comment on the above draft guidelines.

The International Society for Pharmaceutical Engineering (ISPE) is an individual membership Society of more than 20,000 professionals involved in the manufacture of pharmaceuticals and related products. All scientific and technical areas of the pharmaceutical manufacturing industry are represented among the ISPE Membership. ISPE is committed to creating a forum for uniting the world's pharmaceutical manufacturing community and regulators.

In the apparent absence of a standard EC comment form we have utilised a generic template and trust this is acceptable. ISPE is pleased to make both general and specific comments to the guideline as detailed in the attachment to this letter.

Yours sincerely,

President/CEO, ISPE

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ENGINEERING PHARMACEUTICAL INNOVATION

Regulatory Comment Form

Proposed Regulation/Guidance Document: ***Guidelines on the Principles of Good Distribution Practice for Active Substances for Medicinal Products for Human Use;*** **Ref. Ares (2013)148102 - 05/02/2013**

Comments Submitted by: ISPE – International Society for Pharmaceutical Engineering

General Comments
The need to maintain a quality system is indicated but there is no reference to management review of the quality system. Risk Management principles as part of a quality system are referred to (e.g. in item 3) but not explained. That the quality system should extend to all outsourced activities is implied but not explicitly stated. In respect of the above the text should be more harmonised with the recently approved EU-GDP for medicinal products.

No.	SECTION	COMMENT / RATIONALE	PROPOSED CHANGE (IF ANY)
1	Personnel Point 6	Use the male and female terms he/she.	Change the last sentence in Point 6 to read "**He/she** should fulfill **his/her** assigned responsibilities."
2	Personnel Point 7	More appropriate terminology	Replace the word "guarantee" with "ensure": "Key personnel involved in the warehousing of active substances should have the appropriate ability and experience to ~~guarantee~~ **ensure** that active substances are properly stored and handled."
3	Documentation Point 9	Reference to Chapter 5.4 included in the point 9 is erroneous.	Change "Chapter 5.4" to "Chapter 4": "All documentation should be made available on request of competent authorities. Electronic documentation should comply with Chapter ~~5.4~~ **4** of Part II of Eudralex…"
4	Records Point 12	The retention period of "5 years at least" for records in Point 12 should be clarified to avoid misinterpretation.	Change "Records should be clear and readily available. They should be retained for a period of five years at least." to: "Records should be clear and readily available. They should be retained for a period of five years ~~at least~~ **from the last date of distribution or expiration of the active substance batch, whichever is later**."

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5	Records Point 13	It would be desirable to include any deviations / exceptions noted during transportation and receipt of batches in the records under Point 13.	Under "Documents that should be retained and available include:" at the end of the list insert "**Deviations/Exceptions from the prescribed quality system.**"
6	Storage Point 18	Please clarify what is meant by other goods. Should this refer to "other non-pharmaceutical goods"?	"Active substances should normally be stored apart from other **non-pharmaceutical** goods..."
7	Storage Point 20	More appropriate terminology	Replace "attack by" with "growth of" : "Adequate precautions should be taken against spillage or breakage, ~~attack by~~ **growth of** micro-organisms and cross contamination.
8	Storage Point 21	First expiry, first out is only one example of materials management	Add "for example" after "first out": "There should be a system to ensure stock rotation ('first expiry (retest date) first out', **for example**) with regular and frequent checks…"
9	Storage Point 22	The decision to withdraw & destroy product should be made after a full investigation	Add " A full investigation should be performed": "Active substances with broken seals, damaged packaging, or suspected of possible contamination should, be withdrawn from saleable stock. **A full investigation should be performed** and if not immediately destroyed, they ... "
10	Storage Point 23	Point 23 requires clarification as the sentence does not read correctly	

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11	Deliveries to customers Point 25a	More appropriate terminology	Change “not lost” to “maintained at all times”: “their identification is ~~not lost~~ **maintained at all times**;”
13	Deliveries to customers Point 25d	More appropriate terminology	Replace “attack by” with “exposure to” : “they are secure and not subjected to unacceptable degrees of heat, cold, light, moisture or other adverse influence, nor to ~~attack by~~ **exposure to** microorganisms or pests.”
14	Returns Point 34	Any decision to destroy material should be made after a full investigation	Add “after a full investigation” “If the conditions under which returned active substances have been stored or shipped before or during their return or the condition of their containers casts doubt on their quality **after a full investigation** they should be destroyed by appropriate means.”
15	Returns Point 38	First expiry, first out is only one example of materials management	Modify the last sentence to read: “Active substances returned to saleable stock should be placed such that the ~~'first expiry (re-test date) first out' system operates effectively~~ **normal rotation system (for example, “first expiry (retest date) first out” system) operates effectively.”**

No.	SECTION	COMMENT / RATIONALE	PROPOSED CHANGE (IF ANY)
16	Complaints and Recalls Points 39-46	Point 39: This procedure should include how a complaints is to closed and if necessary re-opened	Add after "...procedure". "**This procedure should include how a complaint is to be opened, how a previously closed complaint might if appropriate be reopened and how a complaint should be closed."**
		Point 41: Include the investigation reports to be archived as part of the complaint records.	Add after "corrective action." "**All investigation reports should be archived with the associated complaints record**"
		Point 44: Emphasise urgency to inform for this particular event	Add "immediately" after "informed": "In the event of a serious or potentially life-threatening situation, local, national, and/or international authorities should be informed **immediately** and their advice sought."
		Point 45: Include in the recall procedure who is responsible for the recall decision and the timelines for communication of the recall decision to the concerned local, national and/or international authorities and original manufacturer/customers from the time the recall decision is initiated.	Add after "...considered." "**This procedure should detail who is responsible for the recall decision and appropriate timelines for communication of the recall decision to the concerned local, national and/or international authorities and original manufacturer and customers from the time the recall decision is initiated."**
		Point 46 should include the requirements in the Recall procedure for how a recall should be closed.	Add "**and closed**" after "initiated"

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17	Self-inspections	The sequential number for this item is incorrect.	