EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

27 Sep 2011

Submission of comments on ' ICH Q11, Development and Manufacture of Drug Substances (Chemical Entities and Biotechnological/ Biological Entities)', (EMA/CHMP/ICH/425213/2011)

Comments from:

Name of organisation or individual
The Bulk Pharmaceutical Task Force (BPTF), an affiliate group of Society of Chemical Manufacturers and Affiliates (SOCMA)

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)*
	N/A	

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)*
Section 3.1.4., third paragraph, second sentence		Comment: To clarify examples of impurities applicable to chemical entities in a format similar to that used for biotechnological/ biological immediately following, a wording revision is recommended. Proposed change (if any): Revise to read: For chemical entities, impurities can include organic impurities (e.g., process-related impurities, potential degradation impurities, and including potential genotoxic impurities), inorganic impurities, (~~for example~~ e.g., metal residues,) and residual solvents (see ICH Q6A, Q3A, and Q3C).	
Section 3.1.6., first paragraph, last sentence		Comment: The sentence regarding the need for process validation seems "out of place" relative to the paragraph's discussion on process development and use of design space. The need for process validation is discussed in section 7; if this concept needs to be highlighted, it should be discussed in Section 7. Proposed change (if any): Delete the last sentence.	

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Section 3.1.6., second paragraph, last sentence		Comment: The use of "multiple" is redundant with the plurality of "operations". Proposed change (if any): Revise to read: All steps (or unit operations) should be evaluated to establish appropriate acceptance criteria for impurities as they progress through ~~multiple~~ process operations.	
Section 3.2.3., second paragraph, first sentence		Comment: The changes have been implemented, therefore the data (e.g., impurity profiles, etc.) should exist to provide an actual assessment of the change impact. Proposed change (if any): Revise to read: The reason for each significant change should be explained, together with an assessment of its ~~potential to~~ impact on the quality of the drug substance (and/or intermediate, if appropriate).	
Section 3.2.4., second paragraph, last sentence		Comment: The option to summarize or reference extensive information or data should be allowed. Proposed change (if any):	

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		Revise to read: Where development refers to specific prior knowledge, the relevant information and data should be provided, summarized, or referenced and, where appropriate, the relevance to the particular drug substance should be justified.	
Section 5.1.1., third bullet point		Comment: An editorial addition is suggested to clarify that significant "unit operations" should be included as part of the manufacturing process description. Proposed change (if any): Revise to read: Manufacturing steps (or unit operations) that impact the impurity profile of the drug substance should normally be included in the manufacturing process described in Section 3.2.S.2.2 of the application;	
Section 7.1, last paragraph		Comment: Because the entire paragraph is a single sentence, additional punctuation and verbiage are recommended for clarification. Proposed change (if any): Revise to read: As an alternative to the traditional process validation, continuous process verification (ICH Q8) can be utilised in process validation protocols for the initial commercial	

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		production, and also for manufacturing process changes that are implemented for the continual improvement throughout the remainder of the product lifecycle.	
Section 10.1 Example 1, first illustration		Comment: An additional visual aid will provide a clear picture for conditions that are above vs. those that are below the 0.30% acceptance criterion. Proposed change (if any): It is recommended that a dashed or dotted line be added to the graph demarcating the 0.30% level.	
Section 11. Glossary		Comment: To ensure consistency with ICH Q7, and to ensure that the concept that an API can be designated as a starting material for another API's process, it is recommended that the ICH Q7 definition of "API Starting Material" be included in the Glossary. Proposed change (if any): Add the following to the Glossary: **API Starting Material** A raw material, intermediate, or an API that is used in the production of an API and that is incorporated as a significant structural fragment into the structure of the API. An API	

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		Starting Material can be an article of commerce, a material purchased from one or more suppliers under contract or commercial agreement, or produced in-house. API Starting Materials are normally of defined chemical properties and structure.	

Please add more rows if needed.