Sir/Madam

Having reviewed the draft guidelines on the details of the various categories of variations, I attach comments/amendments/suggestions for change.

Kind regards

Nilesh Sheth MRPharmS
Regulatory consultant

Change code	Comments
A5 Change in the name and/or address of a manufacturer of the finished product including importer, batch release or quality control testing sites	**Conditions** 1. The specific site undergoing the name and/or address change ~~including~~ and all manufacturing operations shall remain the same.
B.I.a.4 Change to in-process tests or limits applied during the manufacture of the active substance	**Conditions** 8. The manufacturing process has been developed using an acknowledged enhanced development approach and the changes only concern non critical process parameters. Comment: The phrase 'acknowledged enhanced development approach' has been used several times in the document. This might not be a universally understood term (e.g. acknowledged by whom?) and a reference or further clarification is necessary.

Change code	Comments	
B.I.f.3 Changes to an approved post approval change management protocol related to the active substance	**Conditions** Are there any conditions associated with this change?	
B.II.a.1 Change or addition of imprints, bossing or other markings including replacement, or addition of inks used for product marking	a) Change in imprints, bossing or other marking	**Conditions to be fulfilled** Exclude 3 as it refers to scoring/break lines?
	b) Changes in scoring//break lines intended to divide into equal doses	Include 3 as it refers to scoring/break lines?
B.II.e.1 Change in immediate packaging of the finished products **b) Change in type of container, deletion of pack and/or presentation or addition of a new container** **3) Deletion of a pack and/or presentation that does not lead to the complete deletion of a strength or pharmaceutical form**		

Change code	Comments
B.II.e.5 change in pack size of finished product	**Documentation** In case of multipack/bundle pack, the multipack/bundle pack must ensure that the packs remain together during transportation and in pharmacy and should contain all legally required labelling items for the outer packaging, including blue-box (BB) information. In addition, it should comply with the applicable guidance at EMA/CMD level Comment: The above insertion is not easily understood e.g. 'Bundle pack' is not a well recognised term. Suggest that the insertion is amended to clarify the message to be conveyed here. All packs will be individually labelled with the legally required labelling, so what is the significance of the stipulation that the packs must remain together during transport etc. particularly if the packs are going to be dispensed individually from a pharmacy?
B.III.1 Submission of a new or updated Ph. Eur. certificate of suitability or deletion of Ph. Eur. certificate of suitability: **-For an active substance** **-For a starting material/reagent/intermediate used in the manufacturing process of the active substance** **-For an excipient**	**Conditions** 11. If the active substance is a not a sterile substance but is to be used in a sterile medicinal product then according to the CEP ~~it must not use~~ water must not be used during the last steps of the synthesis of the active substance or if it does, the active substance must also be ~~claimed to be~~ free from bacterial endotoxins.

Change code	Comments
C.I.1 change in the Summary of Product Characteristics or Package Leaflet following a referral procedure in accordance with Article 30, 31, 107g, 107k or 107q of Directive 2001/83/EC or Articles 34 or 35 of Directive 2001/82/EC or Article 29 of Regulation (EC) No 1901/2006 Suggestion: Assuming that the above are all referral procedures, might it not be better to retain the word 'referral' and to add the word 'procedure' for all occurrences i.e. referral procedure?	
From page 85 onwards of the draft document	From page 85 onwards of the draft document, the wording of the change codes and the words 'conditions' and 'documentation' should be in BOLD.

General comment:

- The abbreviation 'EU' and the 'Union' are used throughout the document. On the basis that both of the of these convey the same meaning, might it not be better to use the abbreviation 'EU' throughout the document as this is probably the more universally understood term?