Proposals to Variation Regulation (version 24.10.2007)

	Current redaction	**Proposed**	**Reason/remarks**
Page 7 Chapter II 8. Article 1.(b)	*within twelve months following implementation of the variation in the other cases.*	*within two months following a calendar year about the implemented minor variations in the previous year.*	EUGMP 1.5. (V) recommends that Annual Product Quality Review should be prepared about previous year
Page 10 Chapter III 12. Article 1.(b)	*within twelve months following implementation of the variation in the other cases.*	*within two months following a calendar year about the implemented minor variations in the previous year.*	
Page 14 Chapter IV 17. Article 1.(b)	*within twelve months following implementation of the variation in the other cases.*	*within two months following a calendar year about the implemented minor variations in the previous year.*	
	DRAFT DETAILED GUIDELINE REFFERED TO IN ARTICLE 6(1)(a): CONDITIONS FOR CLASSIFICATION OF VARIATIONS		
Page 27	A variation which is classified in this guideline but which does not fulfil all the necessary conditions laid down in the relevant subcategory shall be considered to be of Type II.	A variation which is classified in this guideline but which does not fulfil all the necessary conditions laid down in the relevant subcategory, (e.g. removal or widening of quality indicating parameters, changes of principles of manufacturing technology, changes to less protective primary packaging materials etc. shall be considered to be of Type II if such possibility had not been included in the marketing authorization application.	Explanation: The most usual cases are listed

	Current redaction	Proposed	Reason/remarks
	7. Replacement or addition of a manufacturing site for part or all of the manufacturing process of the finished product		
Page 28 **7**. b.3.	3. **Liquid pharmaceutical forms (*e.g.* suspensions, emulsions)** Conditions: 1,2,3,4,5 **Type:IB**	3. **Liquid pharmaceutical forms (*e.g.* suspensions, emulsions)** Conditions: 1,2,3,4,5 **Type:IA**	According to condition 1, compliance with GMP is mandatory
Page 29 **10.**	**10. Minor change in the manufacturing process of the active substance Type: IB**	**10. Minor change in the manufacturing process of the active substance Type: IA**	Conditions 1 and 3 and quality specification guarantee quality and safety of API. Minor changes are practically the Qualified Person's responsibility**.**
	13. Change in test procedure for active substance or starting material, intermediate, or reagent used in the manufacturing process of the active substance		
Page 31 **13**.b.	**b. Other changes to a test procedure, including replacement or addition of a test procedure** Conditions 2,3,4,5 **Type IB**	**b. Other changes to a test procedure, including replacement or addition of a test procedure** **for active substance** Conditions 2,3,4,5 **Type IB** **for starting material, intermediate, reagent** Conditions 2,3,4,5 **Type IA**	Excluded changes to test procedures of reagents and intermediates.

	Current redaction	Proposed	Reason/remarks
	20. Change in test procedure for an excipient		
Page 34-35 **20**.c.	**c. Other changes to a test procedure, including replacement of an approved test procedure by a new test procedure.** Conditions 2,3,~~4,5~~ **Type IB**	**c. Other changes to a test procedure, including replacement of a non-critical approved test procedure by a new test procedure.** Conditions 2,3~~,4~~,5 **Type IA**	Test procedures for excipients are very specific and often could only be performed in special laboratories. After the validation of processes and qualification of excipients manufacturers, non-critical test procedures for excipients may be omitted.
Page 34-35 20. c.5.	Conditions: ~~5. The substance is not a biological excipient~~	5. Excipient manufacturer and supplier shall be qualified or audited	A responsibility of the Marketing Authorization Holder.