Annex to the EFPIA/VE response to the European Commission's proposals for amendments to Regulation 1234/2008. Alternative wording proposals highlighted in the text below with accompanying rationale.

Amendments to Regulation 1234/2008			
Article	**Current Wording**	**Proposed alternative wording**	**Rationale**
Article 6a	*For certain changes to the chemical, pharmaceutical and biological information for a medicinal product a holder may rely on a range of process parameters, quality attributes or summary protocols, upon agreement of the relevant authority and subject to the conditions referred to in the Annexes and the guidelines referred to in Article 4(1) with regard to the specific regulatory tool.*	*For certain changes to the chemical, pharmaceutical and biological information for a medicinal product a holder may rely on a range of process parameters, quality attributes or summary protocols, upon agreement of the relevant authority and subject to the conditions referred to in the Annexes and the guidelines referred to in Article 4(1) with regard to the specific regulatory tools e.g., design space, post approval change management protocols and others as science and technology progresses.*	We understand that the intention of this Article is to formalise the legal basis for 'additional regulatory tools' such as design space and post-approval change management protocols (PACMPs), which are currently only in the annex or guidelines. Whilst this new article is welcomed, we are proposing minor additional wording to aid overall understanding of the intent of the article. Additional wording is also proposed for inclusion in Annex II to provide further support to these points.
Article 7(2)(a)	*where the same minor variation or variations of type IA to the terms of the same marketing authorisations owned by the same holder are notified at the same time to the same relevant authority, a single notification as referred to in Article 8 or 14 may cover all such variations.*	*Where ~~the same~~ multiple minor variations ~~or variations of type 1A~~ to the terms of the same marketing authorisation~~s~~ owned by the same holder are notified at the same time to the same relevant authority, a single notification as referred to in Article 8 or 14 may cover all such variations*	Proposed edits for clarity.
Article 20, paragraph 1	*By way of derogation from Articles 7(1) and Articles 9, 10, 13b, 13c, 13d, 15 and 16 the holder shall follow the worksharing procedure laid down in paragraphs 3 to 9 of this Article in the following cases*	*By way of derogation from Articles 7(1) and Articles 9, 10, 13b, 13c, 13d, 15 and 16 the holder ~~shall~~ may follow the worksharing procedure laid down in paragraphs 3 to 9 of this Article in the following cases*	With reference to worksharing, it may be necessary on some occasions to deviate from the worksharing approach. Proposal to revert to the wording in the current version of the regulation, which provides the necessary flexibility to do this in certain cases.

Amendments to Regulation 1234/2008 - Annexes			
	Current Wording	**Proposed alternative wording**	**Rationale**
Annex I (point 1(c))	*replacement of a biological active substance with one of a slightly different molecular structure where the efficacy or safety characteristics are not significantly different, with the exception of the following:*	*replacement of a biological active substance with one of a slightly different molecular structure where the efficacy and/or safety characteristics are not significantly different, with the exception of the following:*	Proposal to revert to the wording in the current version of the regulation, which was considered clearer.
Annex II (general)		*A variation whose classification is not determined by a product lifecycle document agreed by the relevant authority shall be classified as follows:*	Proposal to include additional new text at the start of Annex II to enable more flexibility for variation classification in relation to product lifecycle documents.
Annex II (points 1(g) and 2(n))	*the following point (g) is added:* *'(g) changes related to medical devices and in vitro diagnostic medical devices used in combination with the medicinal product that have no impact on the quality, safety or efficacy of the medicinal product.';*	*the following point (g) is added:* *'(g) changes related to medical devices ~~and in vitro diagnostic medical devices~~ used ~~in combination~~ with the medicinal product (as an integral combination or in exclusive use with) that have no impact on the quality, safety or efficacy of the medicinal product.';*	Proposal to revise the text related to medical devices and in vitro diagnostic medical devices. In situations concerning co-packaged medical devices (or those that are referenced) the lifecycle management of the medical device itself is generally not in-scope (as this is managed separately through the medical device registration/approval [CE Mark]) unless changes in the medical device impact on its use with the particular medicinal product. Further, since there is the potential to include information and evidence about the medical device within the marketing authorisation of the medicine, if a change in the device impacts this, then a variation would be expected. Existing guidance is also currently silent regarding integral device constituents of medicinal products, so this proposal is now inclusive of this, and consistent with the future-state if the proposed definitions within the draft general pharmaceutical legislation are implemented. There is already a separate parallel process for the IVD/companion diagnostic life cycle management (similar to devices) including a consultation process with EMA where applicable. Furthermore, the marketing authorisation for medicinal products does not include information on the IVD/CDx, (nor does the labelling for the medicinal product it is being used with).
	(n) added *changes related to medical devices and in vitro diagnostic medical devices used in combination with the medicinal product that may have a significant impact on the quality, safety or efficacy of the medicinal product.';*	*(n) added* *changes related to medical devices ~~and in vitro diagnostic medical devices~~ used ~~in combination~~ with the medicinal product (as an integral combination or in exclusive use with) that may have a significant impact on the quality, safety or efficacy of the medicinal product.';*	
Annex II (point 2(f))	*variations related to the introduction of a new design space where the design space has been*	*variations related to the introduction of a new design space where the design space has been developed in accordance with the relevant*	Proposal to include additional text which we believe could go further and only reference introduction of a design space as a type II variation where this 'may have a significant impact on the quality, safety or

	developed in accordance with the relevant European and international scientific guidelines	*European and international scientific guidelines and where this may have a significant impact on the quality, safety or efficacy of the medicinal product.*	efficacy of the medicinal product.' We believe this would be in keeping with risk-based approaches described in ICH guidance and can be described more fully in the guideline