Annex 4 of the Guideline for Variation

Safety and Efficacy Changes

	Description of Change	Conditions to be fulfilled	Documentation required	Reporting Type
50	**Change(s) in the Summary of Product Characteristics, Labelling or Patient Information Leaflet of a generic/hybrid medicine following assessment of the same change for the reference product**			
50 a	Implementation of change(s) for which no new additional data is required to be submitted by the MAH	None	1, 2	**Vmin**
50 b	Implementation of change(s) which require to be further substantiated by new additional data to be submitted by the MAH (e.g. comparability)	None	1, 2, 3	**Vmaj**
	Conditions to be fulfilled None			
	Documentation required 1 Attached to the cover letter of the variation application: Reasoning for the applied change (*generics following innovator's change in product information*) 2 Revised product information in track changes and as clean version 3 Data substantiating the applied changes			
51	**Change(s) in the Summary of Product Characteristics, Labelling or Patient Information Leaflet of human medicines intended to implement the outcome of a procedure concerning PSUR/PBRER or PASS, or the outcome of the assessment done by the MCA**			
51 a	Implementation of wording agreed by the NMRA	1	1, 2	**IN**
51 b	Implementation of change(s) which require to be further substantiated by new additional data to be submitted by the MAH	None	2, 3	**Vmaj**
	Conditions to be fulfilled 1 The variation implements the wording requested by the NMRA and it does not require the submission of additional information and/or further assessment			

	Description of Change	Conditions to be fulfilled	Documentation required	Reporting Type
	Documentation required 1 Attached to the cover letter of the variation application: reference to the agreement/assessment of the NMRA 2 Revised product information 3 Data substantiating the applied changes			
52	**Change(s) in the Summary of Product Characteristics, Labelling or Patient Information Leaflet due to new quality, non-clinical, clinical or pharmacovigilance data**			
52		None	1, 2, 3	**Vmaj**
	Note: this variation does not apply when the new data has been submitted under variation 51. In such cases, the change(s) in the SmPC, labelling and/or Patient Information Leaflet is covered by the scope of variation 51			
	Conditions to be fulfilled None			
	Documentation required 1 Attached to the cover letter of the variation application: reference to the agreement/assessment of the MCA 2 Revised product information 3 Data substantiating the applied changes			
53	**Change in the legal status of a medicine**			
53	All legal status changes	None	1-2	**Vmaj**
	Conditions to be fulfilled None			
	Documentation required 1 Attached to the cover letter of the variation application: proof of authorisation of the legal status change (e.g. reference to change in category of distribution, product classification e.g. change in orphan designation) 2 Revised product information			
54	**Change(s) to therapeutic indication(s)**			
54 a	Addition of a new therapeutic indication or modification of an authorised one	None	None	**Vmaj**
54 b	Deletion of a therapeutic indication	None	None	**Vmin**
	Note: where the change takes place in the context a variation for a generic product — when the same change has been done for the reference product, variations 50 apply.			
	Conditions to be fulfilled None			

	Description of Change	Conditions to be fulfilled	Documentation required	Reporting Type
	Documentation required None			
55	**Deletion of:**			
55 a	pharmaceutical form	None	1, 2	**Vmin**
55 b	strength	None	1, 2	**Vmin**
	Conditions to be fulfilled None			
	Documentation required 1 Declaration that the remaining product presentation(s) are adequate for the dosing instructions and treatment duration as mentioned in the Summary of Product Characteristics 2 Revised product information			
	Note: in cases where a given pharmaceutical form or strength has received a marketing authorisation which is separate to the marketing authorisation for other pharmaceutical forms or strengths, the deletion of the former will not be a variation but the withdrawal of the marketing authorisation. In cases where a given pharmaceutical strength has separate Summary of Product Characteristics for each marketing authorisation this variation is not applicable			
56	**Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the risk management plan**			
56 a	Implementation of wording agreed by the MCA	1	1-2	**IN**
56 b	Implementation of change(s) which require to be further substantiated by new additional data to be submitted by the MAH where significant assessment by the MCA is required (*)	None	None	**Vmaj**
	Conditions to be fulfilled 1 The variation implements the action requested by the authority and it does not require the submission of additional information and/or further assessment			
	Documentation required 1 Attached to the cover letter of the variation application: A reference to the relevant decision of the NMRA 2 Update of the relevant section of the dossier			
	Note: this variation covers the situation where the only change introduced concerns the conditions and/or obligations of the marketing authorisation, including			

	Description of Change	Conditions to be fulfilled	Documentation required	Reporting Type
	the risk management plan and the conditions and/or obligations of marketing authorisations under exceptional circumstances and conditional marketing authorisation (*) the introduction of a risk management plan requested by the NMRA always requires significant assessment			
57	**Other variations not specifically covered elsewhere in this guideline which involve the submission of studies to the MCA (*)**			
57		None	None	**Vmaj**
	Conditions to be fulfilled None			
	Documentation required None			
	Note: in cases where the assessment by the NMRA of the data submitted leads to a change of the Summary of Product Characteristics, Labelling or Patient Information Leaflet or the relevant amendment to the Summary of Product Characteristics, Labelling or Patient Information Leaflet is covered by the variation. (*) This variation does not apply to variations that can be considered as Vmin by default under any other section of this guideline			
58	**Changes to the Labelling or Patient Information Leaflet which are not connected with the Summary of Product Characteristics**			
58 a	Administrative information concerning the MAH‘s representative	None	1	**IN**
58 b	Other changes	None	1	**Vmin**
	Conditions to be fulfilled None			
	Documentation required 1 Revised product information			