Annex 1 of the Guideline for Variation

Administrative changes and Changes to a CEP or to a confirmation of API-prequalification document

	Description of Change	Conditions to be fulfilled	Documentation required	Reporting Type
1	**Change in the name and/or corporate address of the MAH of the FPP**			
1		1	1	**IN**
	Conditions to be fulfilled 1 Confirmation that the MAH of the product remains the same legal entity			
	Documentation required 1 A formal document from a relevant official body (e.g. NMRA) in which the new name and/or address is mentioned			
2	**Change in the name or address of a manufacturer of an API**			
2		1	1-2	**IN**
	Conditions to be fulfilled 1 No change in the location of the manufacturing site and in the manufacturing operations			
	Documentation required 1 A formal document from a relevant official body (e.g. NMRA) in which the new name and/or address is mentioned 2 An updated Letter of Access in case of change in the name of the holder of the APIMF			
3	**Change in the name and/or address of a manufacturer of the FPP**			
3		1	1	**IN**
	Conditions to be fulfilled 1 No change in the location of the manufacturing site and in the manufacturing operations.			
	Documentation required 1 Copy of the modified manufacturing authorization or a formal document from a relevant official body (e.g. NMRA) in which the new name and/or address is mentioned			
4	**Deletion of a manufacturing site or manufacturer involving:**			
4 a	production of the API starting material	1	1	**AN**
4 b	production or testing of the API intermediate or API	1-2	1	**IN**

	Description of Change	Conditions to be fulfilled	Documentation required	Reporting Type
4 c	production, packaging or testing of the intermediate or FPP	1-2	1	**IN**
	Conditions to be fulfilled 1 At least one other site continues to perform the same function(s) as the site(s) intended to be deleted 2 The deletion of the site is not a result of critical deficiencies in manufacturing			
	Documentation required 1 Clear identification of the manufacturing, packaging and/or testing site to be deleted, in the letter accompanying the application			
Changes to a CEP or to a confirmation of API-prequalification document				
5	**Submission of a new or updated CEP for an API or starting material or intermediate used in the manufacturing process of the API:**			
5 a 1)	from a currently accepted manufacturer	1-5	1–5	**AN**
5 a 2)		1-4	1–6	**IN**
5 a 3)		1, 3-4	1–6	**Vmin**
5 b 1)	from a new manufacturer	1–4	1–6	**IN**
5 b 2)		1–4	1–6	**Vmin**
	Conditions to be fulfilled 1 No change in the FPP release and shelf-life specifications 2 Unchanged (excluding tightening) additional (to Ph. Eur.) specifications for any impurities including organic, inorganic and genotoxic impurities and residual solvents, with the exception of residual solvents when the limits stipulated comply with ICH requirements 3 The manufacturing process of the API, starting material or intermediate does not include the use of materials of human or animal origin for which an assessment of viral safety data is required 4 For low solubility APIs the polymorph is the same, and whenever particle size is critical (including low solubility APIs) there is no significant difference in particle size distribution, compared to the API batch used in the preparation of the biobatch 5 No revision of the FPP manufacturer's API specifications is required			
	Documentation required 1 Copy of the current (updated) CEP, including any annexes and a declaration of access for the CEP to be duly filled out by the CEP holder on behalf of the FPP manufacturer or applicant who refers to the CEP 2 A written commitment that the MAH will inform MCA in the event that the CEP is withdrawn and an acknowledgement that withdrawal of the CEP will require additional consideration of the API data requirements to support the product dossier			

	Description of Change	Conditions to be fulfilled	Documentation required	Reporting Type
	3 Replacement of the relevant pages of the dossier with the revised information for the CEP submission option stipulated under section 3.2.S of the MCA Guidance on submission of documentation for marketing authorisation (registration): quality part 4 (S.2.5) For sterile APIs, data on the sterilisation process of the API, including validation data 5 (P.8.2) In case of the submission of a CEP for an API, the quality characteristics of the API are changed in such a way that it may impact the stability of the FPP, a commitment to put under stability one batch of the FPP of at least pilot-scale, and to continue the study throughout the currently accepted shelf-life and to immediately report any out-of-specification results to MCA. 6 (S.4.1) Copy of FPP manufacturer's revised API specifications			
6	**Submission of a new or updated confirmation of API-prequalification:**			
6 a 1)	from a currently accepted manufacturer	1–3	1–3, 5	**AN**
6 a 2)		1–2	1–5	**Vmin**
6 b 1)	from a new manufacturer	1–3	1–3, 5	**IN**
6 b 2)		1–2	1–5	**Vmin**
	Conditions to be fulfilled 1 No change in the FPP release and shelf-life specifications 2 For low solubility APIs the API polymorph is the same, and whenever particle size is critical (including low solubility APIs) there is no significant difference in particle size distribution, compared to the API batch used in the preparation of the biobatch 3 There is no difference in impurity profile of the proposed API to be supplied, including organic, inorganic, genotoxic impurities and residual solvents, compared to that of the API currently supplied. The proposed API manufacturer's specifications do not require the revision of the FPP manufacturer's API specifications			
	Documentation required 1 Copy of the current (updated) confirmation of API-PQ document. The API manufacturer should duly fill out the authorisation box with the name of the MAH or FPP manufacturer seeking to use the document 2 Replacement of the relevant pages of the dossier with the revised information for the API-PQ procedure submission option (Option 1: confirmation of API Prequalification document) stipulated under section 3.2.S. of the MCA Guidance on submission of documentation for marketing authorisation (registration): quality part 3 (S.2.5) For sterile APIs, data on the sterilisation process of the API, including validation 4 (S.4.1) Copy of FPP manufacturer's revised API specifications 5 (P.8.2) If the quality characteristics of the API are changed in such a way that it may impact the stability of the FPP, a commitment to put			

	Description of Change	Conditions to be fulfilled	Documentation required	Reporting Type
	under stability one batch of at least pilot-scale of the FPP and to continue the study throughout the currently accepted shelf-life and to immediately report any out-of-specification results to MCA			
7	**Submission of a new or updated transmissible spongiform encephalopathy (TSE) CEP for an excipient or API (addition or replacement)**			
7		None	1	**IN**
	Conditions to be fulfilled None			
	Documentation required 1 Copy of the current updated TSE (CEP)			