B. QUALITY CHANGES

B.I ACTIVE SUBSTANCE

B.I.a) Manufacture

B.I.a.1 Change or addition in the manufacturer of a starting material/reagent/intermediate used in the manufacturing process of the active substance or change in the manufacturer (including where relevant quality control testing sites) of the active substance, where no Ph. Eur. Certificate of Suitability is part of the approved dossier	Conditions to be fulfilled	Documentation to be supplied	Procedure type
l) Change or addition of a manufacturer of a starting material/reagent/intermediate used in the manufacturing process of the final substance which will not have a potential to change important quality characteristics of the active substance, such as qualitative and/or quantitative impurity profile requiring qualification, or physico-chemical properties impacting on bioavailability	1,2,3,4	1,2,3,4,5,6	IB
Conditions			
1. No adverse change in qualitative and quantitative impurity profile or in physico-chemical properties.			
2. For starting materials and reagents the specifications and quality control procedures are identical to those already approved. For intermediates, the specifications, quality control procedures and route of synthesis are identical to those already approved.			
3. The active substance is not a biological/immunological substance or sterile.			
4. Where materials of human or animal origin are used in the process, the manufacturer does not use any new supplier for which assessment is required of viral safety or of compliance with the current *Note for Guidance on Minimising the Risk of Transmitting Animal Spongiform Encephalopathy Agents via Human and Veterinary Medicinal Products.*			
Documentation			
1. Amendment of the relevant section(s) of the dossier (presented in the EU-CTD format or NTA volume 6B format for veterinary products, as appropriate), if applicable.			
2. A declaration from the marketing authorisation holder or the ASMF holder, where applicable, that the synthetic route, quality control procedures and specifications of the starting material/reagent/intermediate in the manufacturing process of the active substance (if applicable) are the same as those already approved.			
3. Either a TSE Ph. Eur. Certificate of Suitability for any new source of material or, where applicable, documentary evidence that the specific source of the TSE risk material has previously been assessed by the competent authority and shown to comply with the current *Note for Guidance on Minimising the Risk of Transmitting Animal Spongiform Encephalopathy Agents via Human and Veterinary Medicinal Products*. The information should include the following: Name of manufacturer, species and tissues from which the material is a derivative, country of origin of the source animals, its use and previous acceptance. For the Centralised Procedure, this information should be included in an updated TSE table A (and B, if relevant).			
4. Batch analysis data (in a comparative tabular format) for at least two batches (minimum pilot scale) of the active substance from the current and proposed manufacturers			
5. Where relevant, a commitment of the manufacturer of the active substance to inform the MA holder of any changes to the manufacturing process, specifications and test procedures of the active substance.			
6. For a manufacturer of intermediate, declarations of manufacture in accordance with the cGMP rules and of willingness to be inspected			

B.I.a.2 Changes in the manufacturing process of the active substance	Conditions to be fulfilled	Documentation to be supplied	Procedure type
g) Change or addition of reagent or solvent in the manufacturing process	1, 2, 3, 4, 5, 6,	1,2,3,4	IA
Conditions			
1. No adverse change in qualitative and quantitative impurity profile or in physico-chemical properties.			
2. The synthetic route remains the same, i.e. intermediates remain the same			
3. The specifications of the active substance or intermediates and the process controls are unchanged.			
4. The change is fully described in the open ("applicant's") part of an Active Substance Master File, if applicable.			
5. The active substance is not a biological / immunological substance.			
6. The change does not refer to the geographical source, manufacturing route or production of a herbal medicinal product.			
Documentation			
1. Amendment of the relevant section(s) of the dossier (presented in the EU-CTD format or NTA volume 6B format for veterinary products, as appropriate), and of the approved Active Substance Master File (where applicable), including a direct comparison of the present process and the new process.			
2. Batch analysis data (in comparative tabular format) of at least two batches (minimum pilot scale) manufactured according to the currently approved and proposed process.			
3. Copy of approved specifications of the active substance.			
4. A declaration from the marketing authorisation holder or the ASMF Holder, where applicable, that there is no change in qualitative and quantitative impurity profile or in physico-chemical properties, that the synthetic route remains the same and that the specifications of the active substance or intermediates are unchanged.			

B.IV Medical Devices			
B.IV.1 Change of a measuring or administration device	**Conditions to be fulfilled**	**Documentation to be supplied**	**Procedure type**
d) Revision in any of the "accompanying documents" of a CE- marked device	1,2	1,2	**IA_{IN}**
Conditions			
1. The intended use of the CE- marked device should not have changed substantially			
2. The indications for use of the CE- marked device should not have changed			
Documentation			
1. Samples of the revised accompanying documents, identifying the changes from the previously approved versions			
2. Justification for change			