Appendix 12-2

Documents for the Application of Registration Changes of Manufacturing Process and Batch Size of Drug Product

1. Application form for post-approval changes, stating the changes between old and new contents.
2. Scientific justification for the changes, detailed change contents, drug product and affected manufacturing sites.
3. Detailed description and evaluation report for the proposed change shall be provided. For the changes of manufacturing process, the comparative data before and after changes shall be provided.
4. In case of a change to the process validation protocol of drug product, the process validation protocol shall be provided. After approval, the manufacturer should conduct validation studies on the first three production batches of drug product, and the manufacturer should retain the process validation report for future inspection.
5. The testing methods and certificate of analysis for the final product.
6. Data of stability tests.
7. The requirement of BE study report or dissolution profile comparison has to comply with Article 46 to support the change of manufacturing process or batch size (Note1), no matter there are BE studies or not in product registration.
8. Changes in batch size for solid oral dosage forms which the registered batch size (Note2) is less than 100,000 dosage units (Note3). Applicant should conduct dissolution profile comparison studies. Based on the provided data and review on case by case basis, BE study may be requested if necessary.
9. If necessary, the Standard Manufacturing and Control Procedures and the amount of all starting materials in the batch record or the batch record of the same lot as the finished product may be requested.
10. The change of bio-pharmaceuticals requires comparability exercise, the manufacturer should conduct and submit the comparability studies in accordance with "Comparability of Biotechnological/Biological Products" guideline.

Note：

1. Apply to all products, not only limited to the products that already have BE study results in product registration.
2. If the product had conducted the BE studies (for registration), the registered batch size refers to the size of biobatch. Otherwise, the registered batch size refers to the size of the representative drug product batch. If the product had not conducted the BE studies, and unable to confirm the registered batch size, refer to the size of validation batch.
3. This case applies to the product for which the size of the biobatch in BE study compiled with the Article 9 of Regulation of Bioavailability and Bioequivalence Studies on 2016 January 1st.