Notices for the application of Plant master file" Form C-3

PMF Checklist for Foreign Pharmaceutical Manufacturer

Form C-3: Full review (For the expansion of manufacturing site, the items which are marked with asterisk are required, and the relevant documents shall be enclosed.)

To which case be applied :All products

Applicant:	**Receipt No.**	**Case Number**
Item	Please complete the checklist item by item and indicate the attachment numbers or the page numbers of **submitted documents**.	reviewer comment
3.1 Pharmaceutical Quality System (Chapter 1 and 9 of Part I and Annex1, Annex 2, 3 and 15)		
3.1.1 Product release procedure		
3.1.1.1 Describe the product release procedure.		
3.1.1.2 For product with short shelf-life (such as radiopharmaceuticals, advanced therapy medicinal products, etc.) and which is released before completion of all quality control, describe alternative methods (such as rapid microbiological methods) of obtaining equivalent data to permit batch certification; procedures for different stages of release shall also be described.		
3.1.2 Describe the procedure for product quality review.		
3.1.3 Describe the procedure for quality assessment and management of supplier.		
3.1.4 Describe the management of deviations and non-conformity, their related investigations, as well as the resultant corrective and preventive actions		
3.1.5 Describe the change control procedure regarding to change in premises, equipment, facilities, products and validations.		
3.1.6 Describe the self-inspection and/or quality inspection procedures.		
3.1.7 Briefly describe the application of Quality Risk Management (QRM) on medicine manufacturing. For the application of sterile		

products, QRM procedures shall ensure protection of the final product from the contamination of microbial, particulate and endotoxin/pyrogen. QRM priorities should include appropriate design of the facility, equipment and processes, followed by the implementation of well-designed procedures, and the application of monitoring systems.		
3.1.8 Describe how senior management effectively oversee the effectiveness of the Pharmaceutical Quality System (PQS).		
*3.1.9 For the application of sterile products, describe the implementation and periodic review process of Contamination Control Strategy (CCS), and outline the elements covered by CCS. (For processes such as FFS, BFS, lyophilization, aseptic connections, and single-use systems (SUS), please also refer to Annex 1 requirements 8.100, 8.114, 8.123, 8.129, and 8.132 respectively.)		
3.2 Organization and Personnel (Chapter 2 of Part I and Annex 1)		
3.2.1 Responsibilities of senior managers and key personnel (the head of production, the head of quality control, the head of quality assurance, and the authorized person for release)		
3.2.2 Employee training		
3.2.2.1 Basic training on theory and practice for personnel, which shall include orientation and on-the-job training programs; describe the GMP-related training and the way of training. Describe also how the training program is established in accordance with personnel needs, the approval of the training program , the assessment of the training effectiveness, and the maintenance of the training records		
3.2.2.2 For sterile product manufacturer, describe the procedure of personnel qualification, including training programs for personnel employed in sterile product manufacturing areas, and qualification protocols for personnel gowning procedures relevant to aseptically prepared products.		
3.2.3 Personnel hygiene requirements		
3.2.3.1 Describe medical examination for new employees, routine medical		

examinations, disease reporting system for operators in the production area, and additional health examinations for operators working in clean areas.		
3.2.3.2 For sterile product manufacturer, describe in detail the requirement of clothing, the gowning procedure and the washing procedure of clothing for each grade of clean area.		
3.3. Premises, Facilities, Equipment (Chapters 3 and 5 of Part I, and Annex 1, 9, and 10)		
3.3.1 Premises design		
*3.3.1.1 Layouts of personnel, materials, products, and waste flow. For the application of sterile products, it shall include the locations of autoclaves, depyrogenation ovens/tunnels, sterile filtration, lyophilizers, isolators/RABS, etc.		
*3.3.1.2 For sterile product manufacturer, describe whether restricted access barrier systems (RABS) or isolators are used in order to reduce the need for critical interventions into Grade A areas, such as robotics and automation of processes. Additionally, any alternative approaches to the use of RABS or isolators should be justified.		
3.3.1.3 Describe the storage and control for printed packaging materials.		
*3.3.2 Heating, ventilation and air conditioning (HVAC) systems		
*3.3.2.1 Briefly describe the HVAC systems in production area.		
*3.3.2.2. Layouts of clean room classification in production area (such as A, B, C, D, CNC, etc.).		
*3.3.2.3 Describe pressure differences between adjacent rooms and indicate air-flow directions in the layout of production area, including isolators/RABS.		
*3.3.3 Water treatment systems		
*3.3.3.1 Schematic drawings of water system (including each treatment unit and circulation pipeline).		
*3.3.3.2 Describe the process water treatment system.		
*3.3.3.3 Describe the disinfection and sterilization of water treatment units and		

pipelines.		
*3.3.3.4 Describe the quality monitoring program of the water (including sampling plans, frequency, test items and acceptance criteria).		
*3.3.4 Describe the type(s) of gas(es) that come in contact with products during the manufacturing process and the monitoring program thereof. For the application of terminally sterilized products, the gas or steam used for product sterilization shall also be included.		
*3.3.5 Environmental control in production areas		
*3.3.5.1 Describe the environmental monitoring program in the production area, such as temperature/humidity, particles, microorganisms, and personnel. For sterile product manufacturer, describe method used for the trend analysis in environmental monitoring.		
*3.3.5.2 Where apply for the aseptic preparation, give a brief description for the procedure of Aseptic Process Simulation (APS) (including but not limited to the frequency of implementation, the categories of the production lines, etc.).		
*3.3.5.3 For sterile product manufacturer, describe the cleaning, disinfection and fumigation procedure in the production area, and list the disinfectants used and the rotation frequency. Disinfection should include the periodic use of a sporicidal agent.		
*3.3.5.4 For manufacturer for liquid, cream, ointment, or aerosol, please describe the design and measures to prevent microbial and other contamination.		
*3.3.6 Manufacturing/testing equipment		
*3.3.6.1 List of major manufacturing (including weighing, processing, packaging, and storage) equipment.		
*3.3.6.2 List of in- process control (IPC) instruments and QC lab equipment.		
3.4. Documentation (Chapter 4 of Part I)		
3.4.1 Describe the procedures of documents preparation, review, approval, distribution, and superseded, and controls for records retention.		

3.4.2 Describe procedures for periodical review of documents.		
3.5 In-Process Control (Chapter 5 of Part I, Annexes 1 and 8)		
3.5.1 For manufacturer of drug product, describe the amount of samples taken from the received starting materials for the identification test(s). Describe the procedures or measures to assure the identity of the contents of each container.		
*3.5.2 Flowchart of major manufacturing steps for the applied dosage form/product/process in this case; and indicate the grades of the production area, major equipment, process parameters and in process control items. If applying for sterile products using a specialized techniques, please specify the equipment/systems involved, such as Form-Fill-Seal (FFS), Blow-Fill-Seal (BFS), closed systems, single-use systems (SUS), etc.		
3.5.3 Describe the measures to reduce the risk of cross contamination and mix-ups when different products are packaged in close proximity.		
3.5.4 Describe the management of rejected projects; in cases of additional handling, such as rework or reprocess, the relevant SOP should be provided.		
*3.5.5 For application of aseptic preparation processes, describe the design of the filtration system, including considerations for additional filtration as close as possible to the filling point using aseptic filters.		
3.5.6 For sterile product manufacturer, describe the procedure for container integrity test (including the sampling plan, frequency, and test methods), and describe the inspection procedure for extraneous contamination or other defects of all filled containers.		
3.6 Quality Control (Chapter 6 of Part I, Annexes 3 and 19)		
3.6.1 Describe the ongoing stability program after the product is introduced to the market.		
3.6.2 Reference sample and retention sample: For manufacturer of drug product, describe the sampling, storage conditions, and-shelf-life period of reference samples (including starting materials, packaging materials, or finished products) and retention samples (finished products).		
3.7. Complaints, Returned Products, and Recalls (Chapters 5 and 8 of Part I and Annex		

3)		
3.7.1 Describe the procedures of handling complaints.		
3.7.2 Describe the procedures of handling returned products.		
3.7.3 Describe the procedures of product recall, and the evaluation of the effectiveness of the arrangements for recalls.		
3.8 Storage and Transportation (Chapter 3 of Part I and Annex 15)		
3.8.1 Describe the storage conditions of dosage form applied.		
3.8.2 Describe procedures to ensure the products were transported in accordance with the pre-defined conditions.		
	Signature (including date of signing)	