MOHW FDA No. 1131102726 Announcement dated May 24, 2024

Notices for the application of Plant master file Form C-4

PMF Checklist for Foreign Pharmaceutical Manufacturer

Form C-4: (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 : ATMPs/ Biological medicinal products/Biological medicinal substances

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
General Items of Annex 2A Products and Annex 2B Products		
*4.1 If personnel or equipment pass from areas where exposure to live micro-organisms, genetically modified organisms, toxins, or animals to areas where other products, inactivated products, or different organisms are handled, please provide the Contamination Control Strategy (CCS).		
*4.2 Decontamination design and measures (e.g., containment design, sterilization, disinfection, virus removal or inactivation measures, etc.)		
4.3 If specific microorganisms exist in the production premises (such as host organisms or anaerobes), please enclose the detecting methods.		
*4.4 Where processes are not closed and there is therefore exposure of the product to the immediate room environment (e.g. during additions of supplements, media, buffers, gases, manipulations during the manufacture of ATMPs, addition of materials or cultures to fermenters and other vessels and sampling), relevant engineering and environmental control measures shall be enclosed.		
*4.5 Where chromatography equipment is used, please describe the following items:		
*4.5.1 The implemented control strategy (adapted to the risks) for matrices, the housings and associated equipment when used in campaign manufacture and in multi-product environments.		
*4.5.2 Please provide the documents describing acceptance criteria, operating conditions,		

regeneration methods, life span, and sanitization or sterilization methods of chromatography columns.		
*4.6 Describe the emergency plan for dealing with accidental release of viable organisms.		
4.7 Supplier Evaluation		
4.7.1 The strategy to ensure biological starting material-and raw materials compliance with TSE regulations, such as cryoprotectants, feeder cells, reagents, culture media, buffers, serum, enzymes, cytokines, and growth factors.		
4.7.2 Briefly describe the risk assessment of contamination of starting materials and raw materials that come in direct contact with manufacturing equipment or products during their passage along the supply chain.		
4.8 The requirement of full traceability where human cell or tissue donors are used, including all substances coming into contact with the cells or tissues through to confirmation of the receipt of the products at the point of use. Please describe the storage duration of traceability records.		
4.9 Management of the banking system of cells and/or viruses seed and/or plasmids and/or vectors, including source of cells/viruses/bacteria, testing, storage (including split stocks), inventory management and stability monitoring.		
4.10 For the following selected product types, describe compliance with the corresponding specific PIC/S GMP guidelines：		
4.10.1 Annex 2A Products:	Y/N	
*4.10.1.1 To minimize process variability and the risks of contamination and cross-contamination, please submit a summary report based on Quality Risk Management (QRM) for the dosage form/product operations of the current application. This report should cover premises and equipment, starting materials and raw materials, and the process, among other aspects.		
*4.10.1.2 Describe the measures taken when concurrently producing two or more different ATMPs/batches in the same area.		
*4.10.1.3 Describe the precautions for the safe handling and storage of products with positive serological markers, as well as procedures for working with infectious		

materials.		
4.10.1.4 Describe the sampling and storage procedures for reference samples from starting materials, raw materials, packaging materials and the finished product.		
4.10.1.5 If the following specific types of products are applied, briefly describe the manufacturing process is met the corresponding regulations of PIC/S GMP Annex 2A part B or not:		
a **Animal sourced products**:		
a.1 Starting materials derived from animal sources: other adventitious agents that are of concern (zoonotic diseases, diseases of source animals) should be monitored by an ongoing health programme.		
a.2 Where abattoirs are used to source animal tissues, briefly describe the control measures for pharmaceutical raw materials and how to ensure that these abattoirs provide equivalent levels of control as PIC/S GMP.		
a.3 Describe sources of the cells, tissues, and organs intended for the manufacture of xenogeneic cell-based medicinal products.		
b **Gene Therapy Medicinal Products (GTMPs):** If vector manufacturing is outsourced, please provide documentation regarding the qualification of the vector manufacturer. Additionally, describe the quality control measures applied to the vectors.		
c **Somatic Human and Xenogeneic Cell Therapy Products and Tissue Engineered Products and Combined ATMPs:** Please describe whether the cellular products, bio-molecules, bio-materials, scaffolds, matrices, and other substances are licensed medicinal products or medical devices, or are from other authorized sources.		
4.10.2 Annex 2B Products:	Y/N	
*4.10.2.1 Describe whether control measures to remove organisms and spores are included in the HVAC systems.		
4.10.2.2 If the following specific types of products are applied, briefly describe the manufacturing process is met the corresponding regulations of PIC/S GMP Annex 2B part B or not:		
a **Animal sourced products**:		
a.1 Starting materials derived from animal sources: other adventitious agents that are of concern (zoonotic diseases, diseases of source animals) should be monitored by an ongoing health programme.		
a.2 Where abattoirs are used to source animal		

tissues, briefly describe the control measures for pharmaceutical raw materials and how to ensure that these abattoirs provide equivalent levels of control as PIC/S GMP.		
b **Allergen products:**		
b.1 Describe appropriate biosecurity control measures for colonies (such as of mites or animals) used for the extraction of allergens.		
b.2 Describe sources of allergen extract mixtures.		
c **Animal immunosera products:** Describe control measures for antigens of biological origin.		
d **Vaccines:**		
d.1 Where eggs are used, describe how to assure the health status of all source flocks used in the production of eggs (whether specified pathogen free or healthy flocks).		
*d.2 Describe in which areas vessels containing inactivated products are opened or sampled.		
e **Recombinant products:** For production involving multiple harvests, describe how the period of continuous cultivation is defined and regulated.		
f **Monoclonal antibody products:** Describe control measures appropriate to the different source cells (including feeder cells if used) and materials used to establish the hybridoma/cell line.		
g **Transgenic animal products:** Describe how to ensure that therapeutic products used to treat the animals not to contaminate the product.		
h **Transgenic plant products:** Describe preventive measures against contamination by microbiological agents and cross-contamination with non-related plants, and measures to prevent materials such as pesticides and fertilisers from contaminating the product.		
4.10.3 Medicinal Products Derived from Human Plasma:	Y/N	
4.10.3.1 Describe the duration of storage of retention samples and corresponding records from every pool.		
4.10.3.2 Describe the production control measures for plasma/intermediates of different origins being processed in the same production premises. For example, production in campaigns including clear segregation and defined validated cleaning procedures should be adopted. In the case of contract		

	fractionation programs, state whether dedicated equipment is used in accordance with risk assessment.		
		Signature (including date of signing)	