MOHW FDA No. 1091105341 Announcement dated August 31, 2020 "

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

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 : Biological active substances and medicinal products /Blood products derived from human blood or human plasma

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
4.1. Supplier Evaluation (Annex 2)		
4.1.1. 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.	P.	
4.1.2. 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.	P.	
4.1.3. 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.	P.	
4.2. 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. (Annex 2)	P.	
4.3. 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	P.	

management and stability monitoring. (Annex 2)		
*4.4 Decontamination design and measures (e.g., containment design, sterilization, disinfection, virus removal or inactivation measures, etc.) (Annex 2)	P.	
*4.5 If personnel 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 contamination control measures. (Annex 2)	P.	
*4.6 Describe whether control measures to remove organisms and spores are included in the HVAC systems. (Annex 2)	P.	
4.7 If specific microorganisms exist in the production premises (such as host organisms or anaerobes), please enclose the detecting methods. (Annex 2)	P.	
*4.8 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), relevant engineering and environmental control measures shall be enclosed. (Annex 2)	P.	
*4.9For the manufacturer of biological APIs, please describe the steps for the downstream manufacturing process (e.g., isolation, and purification), control measures adopted, and the environmental classification. (Annex 2)	P.	
4.10 For the manufacturers of medicinal products derived from human blood or plasma, 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. (Annex 14)	P.	
4.11 For the manufacturers of biological APIs, describe the principle on taking and holding reserve/retention samples. (Annex 2)	P.	
4.12 For the manufacturers of medicinal products derived from human blood or plasma, describe the duration of storage of retention samples and corresponding records from every pool. (Annex 14)	P.	
4.13. If the following specific types of products are applied, briefly describe the manufacturing process is metthe corresponding regulations of PIC/S GMP		

Annex 2 part B or not: (Annex 2)		
4.13.1 **Animal sourced products**:		
4.13.1.1. 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.	P.	
4.13.1.2. Describe sources of the cells, tissues, and organs intended for the manufacture of xenogeneic cell-based medicinal products.	P.	
4.13.2 Allergen products:		
4.13.2.1. Describe appropriate biosecurity control measures for colonies (such as of mites or animals) used for the extraction of allergens.	P.	
4.13.2.2. Describe sources of allergen extract mixtures.	P.	
4.13.3 Animal immunosera products: Describe control measures for antigens of biological origin.	P.	
4.13.4 Vaccines:	P.	
4.13.4.1 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).	P.	
*4.13.4.2 Describe in which areas vessels containing inactivated products are opened or sampled.	P.	
4.13.5 Recombinant products: For production involving multiple harvests, describe how the period of continuous cultivation is defined and regulated.	P.	
4.13.6 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.	P.	
4.13.7 Transgenic animal products: Describe how to ensure that therapeutic products used to treat the animals not to contaminate the product.	P.	
4.13.8 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.	P.	
4.13.9 Gene therapy products:		
4.13.9.1 Describe the emergency plan for dealing with accidental release of viable organisms.	P.	

4.13.9.2 Describe control measures to concurrent production of non-viral vectors in the same area.	P.	
4.13.9.3 Describe the shipment of products containing and/or consisting of GMO.	P.	
4.13.10 Somatic and xenogeneic cell therapy products and tissue engineered products: For products with positive serological markers, describe their secure handling and storage procedures.	P.	
	Signature (including date of signing)	