Q&A of Plasma Derived Medicinal Products (PDMPs)

1. **What is a blood product?**
   Answer:
   According to WHO, a blood product is any therapeutic substance derived from human blood, including whole blood and other blood components for transfusion, and plasma-derived medicinal products (PDMPs).

2. **What are plasma-derived medicinal products (PDMPs)?**
   Answer:
   Plasma derived medicinal products are manufactured from human blood plasma (plasma). Plasma can be obtained from whole blood donations (recovered plasma) or by apheresis procedures (source plasma). Plasma is the source of a wide range of medicinal therapeutic products that are used for the treatment and prevention of a variety of life-threatening injuries and diseases often associated with protein deficiency states.

3. **What is a Plasma Master File (PMF)?**
   Answer:
   The PMF is a compilation of all the required scientific data on the quality and safety of human plasma relevant to the medicinal product that uses human plasma in the manufacture. These data cover all aspects of the use of plasma, from collection to plasma pool.

4. **What is the blood establishment?**
   Answer:
   According to WHO Recommendations for the Production, Control and Regulation of Human Plasma for Fractionation, blood establishment is defined as any structure or body that is responsible for any aspect of the collection and testing of human blood or blood components, whatever their intended purpose, and their processing, storage, and distribution when intended for transfusion.

5. **What are the quality requirements for plasma-derived medicinal products (PDMPs)?**
   Answer:
   The quality requirements for PMDPs in general are the same with other biological products, which consist of Chemistry, Manufacturing and Controls (CMC) data of the active substance and finished products as reflected in the Common Technical Document (CTD).
   In particular, as PDMP carry the risk of transmission of blood-borne pathogens, the safety of these products is dependent on the measures taken to minimise the contamination of the starting material (donor selection, screening and testing) and enhanced by the application of virus inactivation procedures and technology that removes or reduces the level of blood-borne viruses and other infectious agents.

6. a. **What is the information contained in the PMF?**
   Answer:
   PMF consists information on the collection and control of the starting plasma material. Such a system aims to ensure quality as well as the traceability of each plasma unit from the donor, through the manufacturing process to the recipient of the product and vice-versa. Documentation should record such information as epidemiological data, the tests performed on the donor, donation, plasma unit, the plasma pool, and post-pooling information on the manufacture and control of the starting material.

b. **What are the requirements for selection of plasma donors?**

Answer:

Plasma for fractionation should be obtained from carefully selected, healthy donors who, after review of the medical history (the donor questionnaire), medical examination, and laboratory blood tests, would be considered not to present an increased risk for transmission of infectious agents by PDMPs.

c. What are tests for screening of plasma donations for infectious markers?

Answer:

- Screening test: HBsAg; anti-HIV; anti-HCV.
- NAT test: test of virus of HCV, HBV, HIV, HAV, and/or B19

Detailed information can be found in WHO Recommendations for the Production, Control and Regulation of Human Plasma for Fractionation.

7. **Can the Drug Substance dossier in Part 2 of ACTD be replaced with PMF?**

Answer:

The PMF only provides information relating to the control of the plasma, including virus inactivation procedures and technology that removes or reduces the level of blood-borne viruses and other infectious agents, to justify its use as a starting material for the medicinal product. This information forms part of Section S.2.3 and Annex A.1 of the ACTD. Hence, the drug substance dossier in Part 2 of ACTD cannot be replaced with the PMF.

8. **Are all changes in the PMF subject to approval by NRA?**

Answer:

All changes in the PMF will require approval by the NRA.

References:

1. WHO Recommendations for the Production, Control and Regulation of Human Plasma for Fractionation (https://cdn.who.int/media/docs/default-source/biologicals/blood-products/ecbs-2005-annex-4-human-plasma fractionation.pdf?sfvrsn=50177626_2&download=true)
2. Guideline on plasma-derived medicinal products EMA/CHMP/BWP/706271/2010 (https://www.ema.europa.eu/en/documents/scientific-guideline/guideline-plasma-derived-medicinal-products_en.pdf)
3. Guideline On The Scientific Data Requirements For A Plasma Master File (PMF) Revision 1. EMEA/CHMP/BWP/3794/03 Rev.1 (https://www.ema.europa.eu/en/documents/scientific-guideline/guideline-scientific-data-requirements-plasma-master-file-pmf-revision-1_en.pdf).
4. Information Sheet: Ensuring the Quality and Safety of Plasma Derived Medicinal Products. (https://cdn.who.int/media/docs/default-source/biologicals/blood-products/infosheet-plasma-derived.pdf?sfvrsn=9b6a9ca9_4&download=true)
5. WHO Guidance on increasing supplies of plasma-derived medicinal products in low- and middle-income countries through fractionation of domestic plasma (https://www.who.int/publications/i/item/9789240021815)