The European Agency for the Evaluation of Medicinal Products
*Pre-authorisation Evaluation of Medicines for Human Use*

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**CPMP POSITION STATEMENT**

# NON-REMUNERATED AND REMUNERATED DONORS: SAFETY AND SUPPLY OF PLASMA-DERIVED MEDICINAL PRODUCTS

## SUMMARY

During the recent Co-Decision Procedure regarding the proposed Blood Directive[1], the European Parliament has raised the question of whether the use of non-remunerated donors is important for assuring the overall safety of plasma-derived medicinal products.

The safety of plasma-derived medicinal products is optimised by the stepwise application, in the course of collection, manufacture and batch release testing, of a number of complementary measures, which are under regulatory control. Both non-remunerated and remunerated donors contribute to the supply with safe plasma-derived medicinal products. Since a very substantial proportion of the total amount of plasma-derived medicinal products used in Europe originate from remunerated donors, a requirement for non-remunerated donors would create major supply problems.

The question of whether or not non-remuneration is important for the safety of blood and blood components for transfusion is a separate issue outside the scope of this document.

## 1. Introduction

The question of whether the use of non-remunerated donors is important for the safety of plasma-derived medicinal products has been raised in the development of the Blood Directive[1]. This document sets out the CPMP position on this question.

## 2. Remunerated and Non-remunerated Donors

### 2.1 Safety considerations

- There is a concern that the information from the donor may not be as reliable if financial compensation is used as an incentive. In the time period before the extent of the HIV disaster and the impact of risk behaviour were fully understood, it was possible that persons in high-risk categories contributed to donations of blood and plasma. Such donors might have been attracted by financial remuneration although HIV infection also occurred in countries with non-remunerated donors. Now the risk factors have been identified and such donors are discouraged. Moreover, donors are now selected through rigorous screening carried out with state of the art techniques.
- The extent to which the risk of an infected donation could, in theory, be influenced by the remuneration of donors varies depending on the infectious agent. (See in particular the discussion on variant Creutzfeldt-Jakob Disease (vCJD) below).
- Requirements for plasma for fractionation, as laid down by the European Pharmacopoeia, are the same with respect to donor selection and testing of plasma regardless of remuneration of donors.
- The safety of plasma-derived medicinal products is ensured by the application of a large number of complementary measures which include inspections of collection and manufacturing facilities, selection of donors, screening of individual donations and testing of pooled plasma units for

[1] Proposal for a European Parliament and Council directive setting standards of quality and safety for the collection, testing, processing, storage and distribution of human blood and blood components and amending Council Directive 2001/83 EEC



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markers of infection with known viruses and, very significantly, the application of validated production processes which are capable of inactivating and/or removing a range of viruses. These measures are under regulatory control through Directive 2001/83/EC. Furthermore, many EU Member States operate a system of release testing of plasma pools and of finished plasma-derived medicinal products by Official Medicines Control Laboratories (OMCL). Risks of infectious diseases due to transmission of infective agents, including pathogens of unknown nature, are minimised by the application of these measures in combination but cannot be absolutely excluded.

- For plasmapheresis donors, including those who are remunerated, there are additional voluntary industry standards to ensure that plasma originates from a low risk donor population. These include qualified donor programs and inventory hold of donations. The greater frequency of donation combined with an inventory hold period increases the likelihood of detecting an infected donation through a look back procedure before its use in the manufacture of medicinal products.
- There is no evidence from clinical studies and pharmacovigilance that donor remuneration increases the risk of viral transmission via plasma-derived medicinal products, which have been subject to proper screening at donation and a validated viral inactivation/removal step.
- The question of whether or not non-remuneration is important for the safety of blood and blood components for transfusion is a separate issue outside the scope of this document.

### 2.2 Supply considerations

- Large volumes of plasma are required for medicinal product, especially immunoglobulin, manufacture. Remunerated plasmapheresis donors contribute a large proportion of the Plasma for Fractionation, as the volume of plasma obtained from non-remunerated donors is quite insufficient to satisfy demand.
- Plasmapheresis can yield large amounts of plasma from a much smaller number of donors because of the high frequency of donation and higher yield per donation.
- Hyperimmune plasma is a special case and is normally only obtained from specially recruited plasmapheresis donors.

Plasma-derived medicinal products licensed in Europe originate from remunerated and non-remunerated donors. It is important to recognise that a very substantial proportion of the total plasma used in the manufacture of plasma-derived products used in Europe originates from paid or remunerated donations. A requirement for unpaid or non-remunerated donors would create major supply problems and product shortages without any justification on grounds of safety.

Shortages of plasma-derived medicinal products have already occurred and patients' associations have expressed concern about decreased availability of essential plasma-derived medicinal products.

### 2.3 Special considerations with respect to vCJD

- The risk of transmission of vCJD by plasma products remains unknown[2]. As a precautionary measure, the use of Plasma for Fractionation sourced from donors in the UK (who, incidentally, were non-remunerated) has been discontinued. The UK is now using US-sourced plasma for the manufacture of their plasma-derived medicinal products.
- Some EU member states are applying exclusion criteria to donors who have spent time in the UK, thus further reducing the European donor population.
- An exclusion of US-sourced Plasma for Fractionation for the reason that the donors are remunerated would result in the exclusion of a population which is recognised as being at low-risk of exposure to BSE (Geographical BSE Risk Assessment) and therefore is at low-risk of developing vCJD.

[2] CPMP Position Statement on New Variant CJD and Plasma-Derived Medicinal Products, CPMP/201/98, 25 February 1998 ( http://www.emea.eu.int/pdfs/human/press/pos/020198en.pdf ). Report of EMEA Expert Workshop on Human TSEs and Plasma-Derived Medicinal Products, CPMP/BWP/1244/00, 27 July 2000 (http://www.emea.eu.int/pdfs/human/regaffair/124400en.pdf ).