

EBA fact sheet on European self-sufficiency for blood components and plasma for fractionation

Context

The European Directive 2002/98/EC on blood and blood components¹ calls for a blood strategy to reinforce confidence in the safety of the blood transfusion chain and to promote Community self-sufficiency. Furthermore, the Directive states that “Member States should take measures [...] to encourage voluntary unpaid donations of blood and blood components.”²

Over the last 10 years, the European Directives on blood and blood components³ have provided a good foundation for the development of sustainable blood transfusion systems in EU Member States. However, challenges to the sustainability of these blood transfusion systems across Europe now require a different and stronger approach on a European scale, at both the strategic and technical levels.

Issues

Self-sufficiency for labile blood components

Keeping a representative donor base in a changing environment

Payments to blood and plasma donors by commercial suppliers erode the current community-based, non-remunerated, donor population, which is the key element to secure a sustainable blood supply. In countries with dual systems (where unpaid and paid collection coexist), blood establishments who collect components for transfusion encounter increasing difficulties in recruiting and retaining unpaid donors.

At the same time, advances in medicine and technology, together with efforts in improving patient blood management, have reduced the demand for the labile key blood component; red blood cells. Notwithstanding this rather positive situation, this poses a challenge for blood establishments.

Indeed, despite the declining demand, blood establishments need to respond to an ever-increasing personalization of components for transfusion (e.g HLA matched, irradiated, virus inactivated for specific patient groups), for a patient population of increasingly diverse ethnic backgrounds. This

¹ DIRECTIVE 2002/98/EC of the European Parliament and of the Council of 27 January 2003 setting standards of quality and safety for the collection, testing, processing, storage and distribution of human blood and blood components and amending Directive 2001/83/EC

² Directive 2002/98/EC, Article 20, Voluntary and unpaid blood donation

³ Directives 2002/98/EC, 2004/33/EC, 2005/61/EC, 2005/62/EC and subsequent amending Directives

requires more focus on the development of a sustainable donor base which fully reflect patients' diverse ethnic backgrounds.

Moreover, outbreaks of emerging infectious diseases, such as the recent Zika virus epidemic, may overwhelm a local donor base, and reinforce the need for collaboration between European blood establishments to ensure continuity of supply throughout Europe.

The risk of “cherry picking” in a context of competition

Commercial suppliers of labile products entering and leaving the market have left some blood supply systems disrupted, both in donor bases and supply. In some Member States, the development of commercial plasma collection centers, using paid donors, is eroding the voluntary donor base for labile blood products and jeopardizes the sustainability of the supply of the full range of blood products.

Several EU Member States have competition between several providers of blood products for the supply of hospitals. While this competition is allowed and sometimes encouraged by national authorities, it often generates a situation of “cherry picking”, where some providers (often with a stated “for-profit” status) choose to only provide the most profitable blood products (e.g. Fresh frozen plasma (FFP) for transfusion) to the most convenient clients (big hospitals, in major cities). In these situations, the incumbent, not-for-profit blood operators tend to remain in charge of ensuring the supply of less profitable or more complex/rare products, delivered to all hospitals including those of small size or located in remote areas.

As a result of this unfair competition, it appears that not-for-profit blood operators are the only who effectively ensure self-sufficiency (even though this specific mission is not necessarily recognized by national law), and who bear the costs of ensuring continuous supply of all products, on all parts of the territory they serve.

Plasma for fractionation into plasma-derived medicinal products

All stakeholders recognize that the EU is not self-sufficient in plasma for fractionation (PfF) and plasma derived medicinal products (PDMP).

As a result, a steadily increasing demand in immunoglobulins generates significant imports of PfF and PDMP from third countries, especially from the United States⁴. This dependency on imports, predominantly from one country, poses a risk to the EU in terms of continuity of supply in crises situations, for example in case of the occurrence in the USA of an outbreak of a transmissible disease, such as variant Creutzfeldt-Jakob disease, or some other emerging infectious disease (EID).

Moreover, a 2012 Presidential order on American national defence resources preparedness foresees that the US Secretary of Health and Human Services can require that national use health

⁴ According to market data, in 2014, 45 million liters of plasma for fractionation were collected worldwide, including 32.6 million liters of source plasma and 8.7 million liters of recovered plasma; 64% of those 45 million liters of available plasma were collected in the USA.

resources (including biological products) be prioritized over the supply of other (foreign) needs and contracts⁵. Should this Presidential order be put into practice for health resources to deal with a major crisis in the United States, the supply of other countries, including in the EU, in PpF and PDMP would be threatened.

EBA proposals for revised Directives

- **Self-sufficiency in labile blood components**

Blood and blood components are critical to many of the operations in the healthcare systems and to the health of recipients. The EBA considers that they should be treated as a strategic resource in the EU.

To ensure sustainability of supply and contingency management, the supply of blood and blood components should be based on proportionate collections in each Member State. The availability of blood and blood components is dependent on the eligible EU population who are prepared to donate. The donor base should be broad, covering the whole population in its diversity, and all Member States. This is the best way to match the trend toward more and more individualised therapeutic transfusion, and to be prepared for outbreaks of emerging infectious diseases, such as the recent Zika virus epidemic, and possible requirements for deferring donors from some regions requiring compensatory supply from other regions.

Member States should ensure that adequate logistics and infrastructures to collect and supply blood and plasma are maintained or developed, and provide guidance on the sustainable use of these resources.

In order to safeguard adequate and equal supply of blood and blood components to all EU inhabitants, based on the needs of the Member States, EU legislation should recognize blood products supply as a service of general interest, for which blood operators (whatever their legal status) should be bound to meet the full spectrum of demand for blood components throughout the national territory in which they operate, or to provide appropriate compensation to those who do. Furthermore, the obligation of supply to special groups of recipients should be evenly shared

⁵ Executive Order -- National Defense Resources Preparedness, 16 March 2012, [The White House](#)
"PART II - PRIORITIES AND ALLOCATIONS [...]"

Sec. 201. Priorities and Allocations Authorities. (a) The authority of the President conferred by section 101 of the Act, 50 U.S.C. App. 2071, to require acceptance and priority performance of contracts or orders (other than contracts of employment) to promote the national defense over performance of any other contracts or orders, and to allocate materials, services, and facilities as deemed necessary or appropriate to promote the national defense, is delegated to the following agency heads: [...]

(3) the Secretary of Health and Human Services with respect to health resources; [...]

PART VIII - GENERAL PROVISIONS [...]

Sec. 801. Definitions. [...]

(i) "Health resources" means drugs, biological products, medical devices, materials, facilities, health supplies, services and equipment required to diagnose, mitigate or prevent the impairment of, improve, treat, cure, or restore the physical or mental health conditions of the population."

between all licensed blood establishments. In order to support enforcement of this measure, further regulation and guidance for Member States should be developed at EU level.

Finally, the criteria of self-sufficiency for blood and blood components for transfusion should be better defined in the Directives, and made a formal requirement of European law.

- **Self-sufficiency in plasma for fractionation and plasma derived medicinal products**

Achieving an agreed level of European self-sufficiency in plasma for fractionation is a key factor in ensuring the long-term supply of plasma-derived medicines needed by patients in the EU.

Quantitative aspect: need for developing efficient plasmapheresis programs

In order to achieve a higher level of self-sufficiency in PfF, the development of plasma collection by apheresis is required.

Available evidence has shown that the efficiency ratios of plasma collection by plasmapheresis in blood establishments are a matter of concern. This has led some countries to specifically develop programmes to improve the efficiency of plasmapheresis collection in blood establishments (e.g. in Denmark, France, Germany, Italy, the Netherlands). Improving the efficiency of plasma collection by apheresis in blood establishments should be regarded as a key factor to get closer to self-sufficiency in PfF and PDMP in the European Union. Member States should be encouraged to stimulate Blood Establishments to develop efficient plasmapheresis collection programmes, based on voluntary non-remunerated donors, to get closer to EU self-sufficiency in plasma for fractionation, for the primary benefit of patients in the EU.

Qualitative aspect: need for reducing wastage of recovered plasma

Reports from the EDQM and studies supported by the European Commission⁶ have established that large volumes of recovered plasma are discarded and lost for fractionation in some EU countries as well as worldwide⁷. The main reason is non-compliance with the quality standards required by the plasma industry in their Plasma Master File (PMF). So far, this issue has been a matter of dispute, because good practice guidelines mentioned in Article 2 of the Directive 2005/62/EC are still awaited. The process aiming to fill this gap is ongoing, with the publication of a Directive amending Directive 2005/62/EC expected by the end of 2016. This evolution, which has been greatly facilitated by the EDQM, and favoured by the EBA for a long time, should be used to develop training programmes with the objective to help blood establishments better comply with the future European good practice guidelines. This would allow to reduce or eliminate the wastage of recovered plasma due to quality concerns.

⁶ An EU-wide overview of the market of blood, blood components and plasma derivatives focusing on their availability for patients, [Creative Ceutical Report](#), revised by the Commission to include stakeholders' comments, 2015

⁷ WHO Drug Information Vol. 27, No. 1, 2013; WHO, Improving access to safe blood products through local production and technology transfer in blood, 2015

Additionally, attention should be paid to the fact that some PMF certification procedure may play a role of economic disincentives to the use of recovered plasma, especially in small countries. Indeed, the costs associated with registering a new source of plasma for fractionation (both direct costs linked to EMA fees, and indirect costs of preparing the registration dossier) are fixed, and can discourage fractionators from accepting smaller amount of recovered plasma. Appropriate mechanisms to limit these economic disincentives (e.g. adjusting PMF registration fees according to the amount of plasma to be delivered) should be explored.

- **Optimizing the use of blood and blood components**

The supply of blood components and PDMP should be determined by the patient or recipient need, like for any other substance of human origin. Overproduction and wastage is ethically questionable and not sustainable. There is a need for controlled clinical trials to demonstrate the optimal use of both blood components and PDMP. These would provide foundations for evidence-based guidelines which should be put in practise by training and auditing programs.

EBA recommendations to DG SANTE

- Blood and blood components, including plasma should be considered a strategic resource, and blood products supply recognized as a service of general interest. European law should require the development and maintenance of adequate infrastructures and donor base by Member States, based on voluntary non-remunerated donation.
- Provisions on the supply of blood and blood products as a service of general interest should require blood service(s) to provide the full spectrum of labile blood components to match the patients' needs. Furthermore, the obligation of supply to special groups of recipients should be shared by all licensed blood establishments.
- Blood establishments should be encouraged to develop efficient plasmapheresis collection programmes, based on voluntary non-remunerated donors in the EU Member States, in order to get closer to EU self-sufficiency in plasma for fractionation, for the primary benefit of patients in the EU.
- The upcoming adoption of an EU Directive amending Directive 2005/62/EC should be taken as an opportunity to develop training programmes for blood establishments, in order to better comply with the future good practice guidelines. This will allow to reduce or eliminate the wastage of recovered plasma due to quality concerns.
- The EU should stimulate research to demonstrate and implement the optimal use of blood, blood components and PDMPs