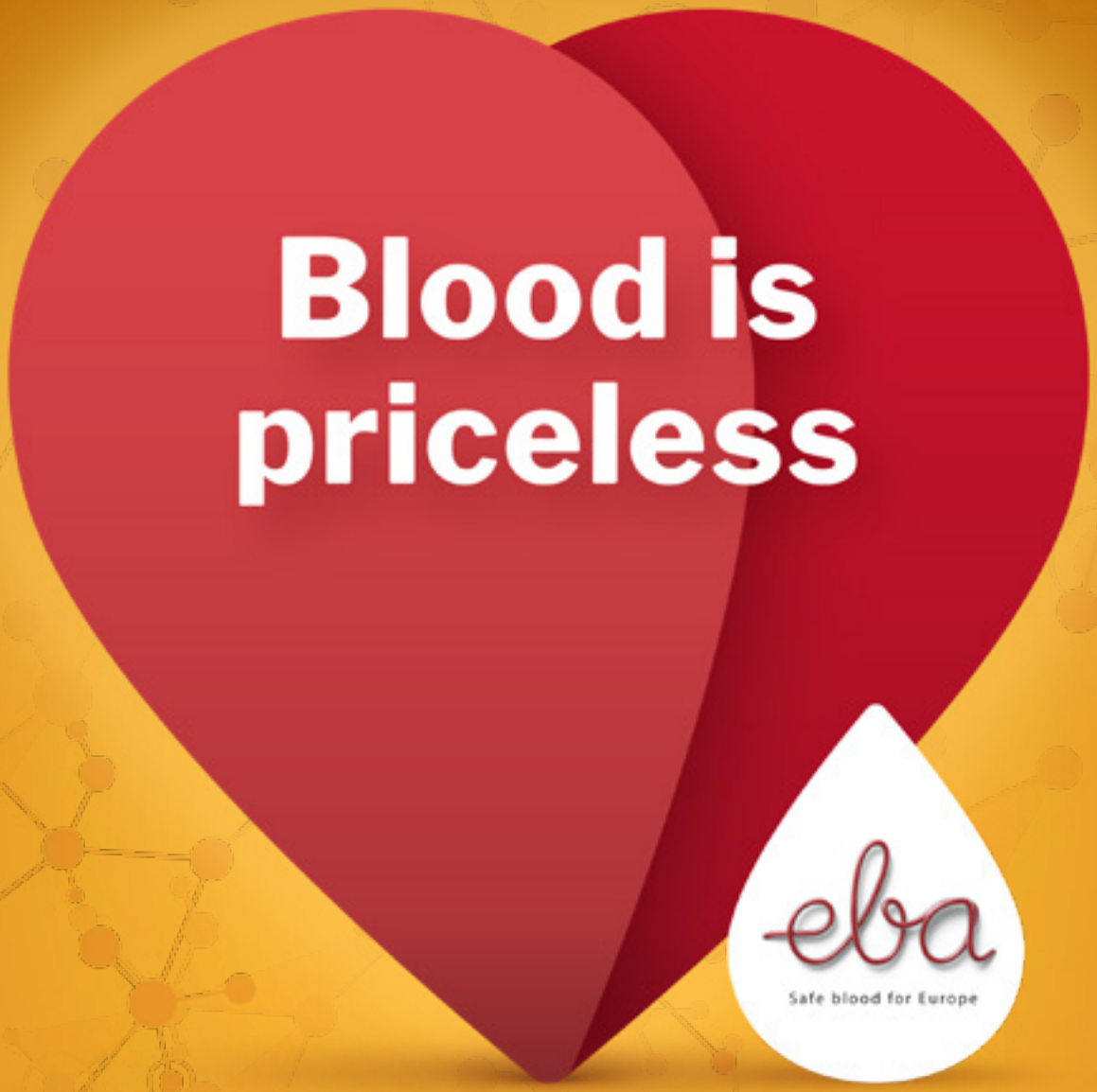


A sustainable blood and blood components provision in the EU – Revision of the EU Blood Directives.

Position Statement

Key recommendations for the future EU legislation
on blood by not-for-profit blood establishments

This European Blood Alliance (EBA) position statement is a call to policy makers in the European Union (EU) to adapt the EU legislation on blood and blood components to the present needs of patients, donors, healthcare professionals, based on the experience acquired with the previous EU legislation.

Providing safe and high-quality blood products, tissue and cells to patients who suffer from trauma, cancer or other conditions requiring transfusion or transplantation is an essential part of contemporary health care. As such, it must be regulated at the European Union level to ensure equity of access to treatment across the Union.

The competence of the European Commission (EC) in this matter is enshrined in the Treaty of the Functioning of the EU (TFEU) art. 168, 4 (a) which states that the EU should adopt "measures setting high standards of quality and safety of organs and substances of human origin, blood and blood derivatives".

As the EC embarks upon the revision of the Blood Tissues and Cells Directives (BTC) on a public health basis, the European Blood Alliance invites decision makers to ensure that this revision guarantees better provision of safe, quality and innovative services to patients who benefit from blood transfusion or blood components in their treatments.

EU Directives, despite some limitations that now need to be addressed, have provided an important and solid foundation for the implementation of standardised methods and practices to achieve high quality and safety of Substances of Human Origin (SoHO).

We call upon European policy makers to take into account the following key issues:

1 Blood is a Human Resource, not a Commodity

Emblematic and sacred, blood can save millions of lives and is a unique and irreplaceable resource coming from voluntary human beings. As such, blood cannot be treated and considered as a mere commodity.

All blood components for therapeutic use should be regulated according to the same principles regardless of the final use of the components, i.e. transfusion or medicinal product manufacture.

2 Importance of Voluntary Non-Remunerated Donation (VNRD)

The principle of Voluntary Non-Remunerated Donation (VNRD) is central to the Blood Tissues and Cells legislation and must remain the basis for any new European legislation. Future European Blood Tissues and Cells Directives must strengthen the implementation of the necessary measures to encourage voluntary and non-remunerated blood donations by Member States. Further, the future Directives should better define compensation for donors of blood, blood components and plasma, through the adoption of the Nuffield Council on Bioethics definition.

3 Need for European Self-Sufficiency

European self-sufficiency on all blood products is necessary to ensure supply meets demands for all patients. Reaching self-sufficiency at EU level requires that plasma (meant for transfusion or for the production of medicines) be qualified as a strategic resource. Furthermore, to reach EU self-sufficiency in plasma-derived products while remaining self-sufficient regarding transfusion blood products and ensuring the highest level of donor protection, the EU should encourage and allow Member States to privilege and support plasma collection by EU non-for profit blood establishments. Further medical training and implementation of evidence-based treatment guidelines is essential to ensure the appropriate use of blood and blood components without excessive application.

4 Need for a Reinforcement of Donor Protection

Donor supply and care are both imperative to the operations of BTC. Providing blood and blood components depends entirely on people's will and ability to save the lives of others by donating blood. Donors must be adequately treated and, as they donate, their health must be protected. Therefore, donor vigilance should be reinforced through a pan-European donor vigilance programme. The EU must encourage Member States to rely on a large donor base with low frequency donations. Relying on a narrow donor base and high frequency donations increases donor burden and is less protective of donor health, while fragilizing self-sufficiency in case of crisis.

5 Principles vs Technical Directions

Bearing in mind dynamic scientific and technical achievements, epidemiological changes and differences between Member States, BTC EU Directives should reassert principles and leave technical provisions to more flexible tools, e.g., Council of European Directorate for the Quality of Medicines and Healthcare (EDQM) guidelines.

6 Need for clarity and coherence

The next set of EU BTC legislation must include clear definitions of roles and tasks for technical bodies, such as the European Centre for Disease Prevention and Control (ECDC) or the EDQM, as well as for mandatory Member States mandates, such as that of quality inspections. Furthermore, Manufacturing standards must be consistent across Europe, independently from the setting (outside hospital, etc.).

1 Blood is a Human Resource, not a Commodity

Blood is essential to everyone's life and it is a "product" quite different from all others, it can save millions of lives as a unique and irreplaceable resource for medicine coming from millions of voluntary human beings. As such, blood cannot be treated and considered as a mere commodity.

A decision of the European Court of Justice[1], focusing on the rules of the EU Internal Market rather than the patients' needs, considered plasma (a blood component) solely as a product, rather than basing its decision on the quality and safety of blood and blood components. **Blood is not a commodity, and decisions on blood components regulations should be made by the legislators and not by judges.**

Blood runs through people's veins, and as such, blood components should only be regulated under public health considerations regardless of the final use of the components (transfusion or medicinal product manufacture). No distinction must be made between different blood components, as they are all critical lifesaving products. Blood components intended for therapeutic use must be regulated and applied consistently across all dimensions. The scope of the new directives should be clearly defined and be applied as the *lex specialis*.

[1]ECJ, 13 March 2014, Octopharma vs. France, Octapharma France SAS v Agence nationale de sécurité du médicament et des produits de santé (ANSM) and Ministère des Affaires sociales et de la Santé, C 512/12.

2 Importance of Voluntary Non-Remunerated Donations

Voluntary Non-Remunerated-Donation[2] is central to BTC legislation and must remain the basis of any new European BTC laws regarding treatment using labile products, tissues and cells.

VNRD is supported by the four principles of bio-medical ethics: autonomy, non-maleficence, beneficence and justice[3]. In the transaction of human bodily materials these principles must be upheld. The Council of Europe Oviedo Convention[4] has strongly encouraged protection of donor's dignity, by prohibiting making the human body and its parts a source of financial gain. The No-financial-gain-principle for the donors and the Blood Establishments must be maintained for all blood products and asserted as fundamental to any health service engaged in blood and blood component supply.

Recently, plasma, as it can be the raw material for medicines, has been the subject of active advocacy, as commercial companies through their trade association[5] argue for a system that will remunerate donors. Though all plasma collectors, including the not-for-profit blood establishments agree that Europe must increase its plasma collection to lessen its dependence on third parties' provider, mainly, the US, the not-for-profit blood establishments argue this aim is achievable without remunerating donors.

Increasing plasma collection by not-for-profit blood establishments, based on VNRD: a paid plasma collection system would carry the risk of eroding the voluntary non-remunerated donor base, which is essential to the supply of blood components for transfusion and which guarantees self-sufficiency in labile blood components.

In line with article 20, paragraph 1, of Directive 2002/98/CE, future European BTC Directives must strengthen the implementation of the necessary measures to encourage voluntary and non-remunerated blood donations by Member States. Further, the future Directives should better define compensation for donors of blood, blood components and plasma, through the adoption of the Nuffield Council on Bioethics definition (a recompense of donors for non-financial losses, e.g., inconvenience, time), as a complement to the classical definition of voluntary non-remunerated donation. The EU must encourage the development and use of tools, such as the intervention ladder of the Nuffield Council on Bioethics[6] , which aims to identify non-altruist-focused forms of compensation for blood, blood component and plasma donors (which are ethically questionable), and altruist-focused forms of encouragement (which are ethically acceptable and compatible with the Council of Europe definition of VNRD).

[2]As part of the Directive 2002/98/EC, 2003: "Member States shall take the necessary measures to encourage voluntary and unpaid blood donations with a view to ensuring that blood and blood components are in so far as possible provided from such donations".
[3]Beauchamp TL, Childress JF: Principles Biomedical Ethics, 5th edn. New York, Oxford University Press, 2001, ISBN 0-19-514332-9 and Folléa G et al. Blood Transfus 2014; 12(Suppl 1):s387–s388.
[4]Convention for the Protection of Human Rights and Dignity of the Human Being with regard to the application of Biology and Medicine: Convention on Human Rights and Biomedicine, 1997
[5]PPTA Statement on Immunoglobulin Use to Meet Clinical Need: "plasmapheresis is a more efficient collection method compared to the collection of recovered plasma, and countries that do not allow remuneration restrict plasma volumes and contribute to Europe's reliance on countries that do"
[6]Nuffield Council on Bioethics, Human bodies: donation for medicine and research, 2011

3 Need for European Self-Sufficiency

European self-sufficiency on all blood products is necessary to ensure EU independence and a high quality of lives for every patient whose health depends on blood or blood products. EBA members are dedicated to achieving this goal. Currently, the European Union relies on the United States for up to 40%[7] of its needs of plasma to manufacture medicines, but impacts such as that of the COVID-19 crisis trigger concerns that local disruptions of plasma supplies could result in regional and global shortages of essential plasma derived medical products (PDMPs).

The next EU legislation should support Member States in reaching and maintaining self-sufficiency, based on Voluntary Non-Remunerated Donations (VNRD) while securing its own market first.

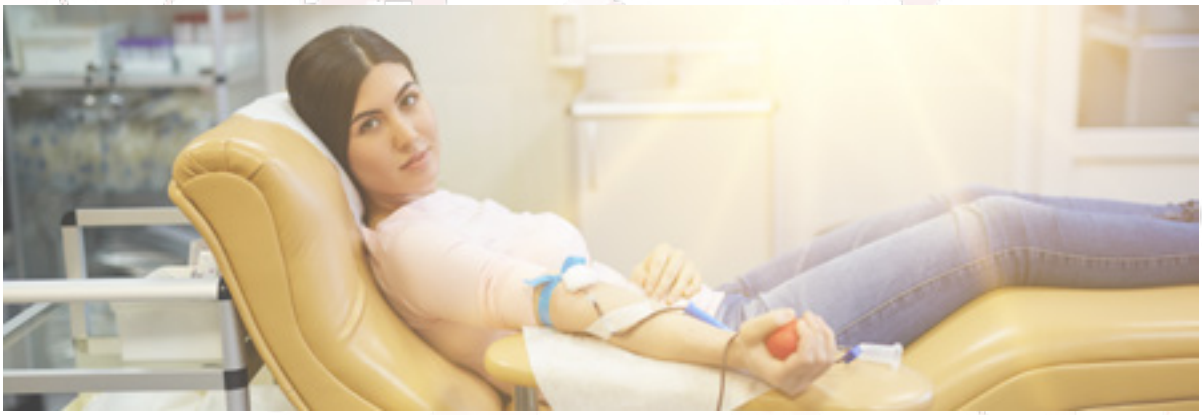
To reach a much-sought after blood and blood products self-sufficiency at the EU level, EBA calls on the EU and Member States to designate plasma as a strategic resource, an "economically important raw material which is subject to a higher risk of supply interruption" and to encourage and allow Member States to privilege and support the not-for-profit sector. The European legislation should set a long-term goal that all plasma donations for fractionation should also come from VNRD and designate a timeframe within which this will be achieved.

This self-sufficiency goal must also rely on best use of blood and blood components through Patient Blood Management (PBM) and enhanced training of medical prescribers who will ensure that the use of BTC is evidence-based and coherent with the latest scientific development.

Education in current science concerning blood transfusion safety and the whole process of blood procurement should be made mandatory in medical training.

Member States must be encouraged to establish transfusion medicine as an independent medical subject with structured training, including programmes for continuous medical education for all medical staff.

Better information of the prescribers would reduce the risk of excessive application of blood and blood components.



[7]As per DG SANTE's presentation made on 21st April at a PPTA online event, this figure is probably less important now that the UK is out of the EU, as the country was the main importer.

4 The Need to Reinforce Donor Protection

Providing blood and blood components depends entirely on people's will and ability to save the lives of others by donating blood. Donors must be adequately treated and, as they donate, their health must be protected.

However, the present EU legislation is not fit for purpose regarding donor selection and deferrals criteria.

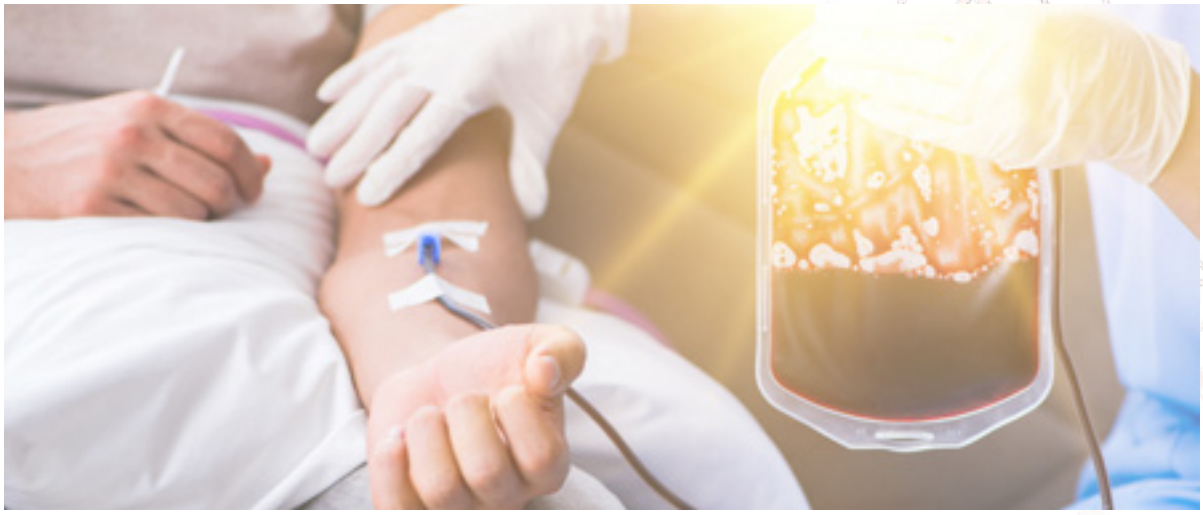
The next EU legislation must make mandatory for all BTC collectors to develop and maintain adequate donor base structures. All licensed blood establishments must supply all components, including to recipients with special or rare needs. The EU must avoid, in particular, the risks at the European level of relying on a narrow plasma donor basis that could, in turn, affect the donor's well-being. The EU should also ensure a robust supply of all blood components for transfusion in case of epidemiological crises.

Relying on a narrow donor base and high frequency donations increases donor burden, is less protective or donor health, reduce donation quality (reduced IgG concentration) while fragilizing self-sufficiency goal and leaving provision of blood and blood products at risk as any crisis or disease will result in a greater number of donor deferrals impacting the collections.

EBA calls on the EU to reinforce donor vigilance requirements through a pan-European donor vigilance programme.

The regulatory landscape has triggered competition between VNRD donors and paid plasma donors. Furthermore, as there is currently no data sharing between the donation centres, EBA's concern is that giving payments to donors may tempt them to approach multiple plasma donations in different centres, putting their health at risk.

The EU must set up a donor vigilance system similar to EudraVigilance. The reporting of data on SoHO should be further developed and should provide public access to key anonymised data on European registries, including clinical follow up, which would support enhanced transparency on donor health. Data across the EU should be pooled, in full compliance with the General Data Protection Regulation (GDPR). Allowing researchers and clinicians access to these registries would be an incentive to improve their reporting and enable practitioners to evaluate the efficacy of SoHO safety measures.



5 Principles vs Technical Directions

As the COVID-19 epidemic has demonstrated, the EU and Member States need a regulatory framework that allows quick adjustment to the circumstances, mostly unforeseen at the time of drafting the legislation, and crisis preparedness to respond to health emergency and to adequately fulfil the needs of patients. In this regard, technical provisions of the EU Blood Directives are too detailed and difficult to change.

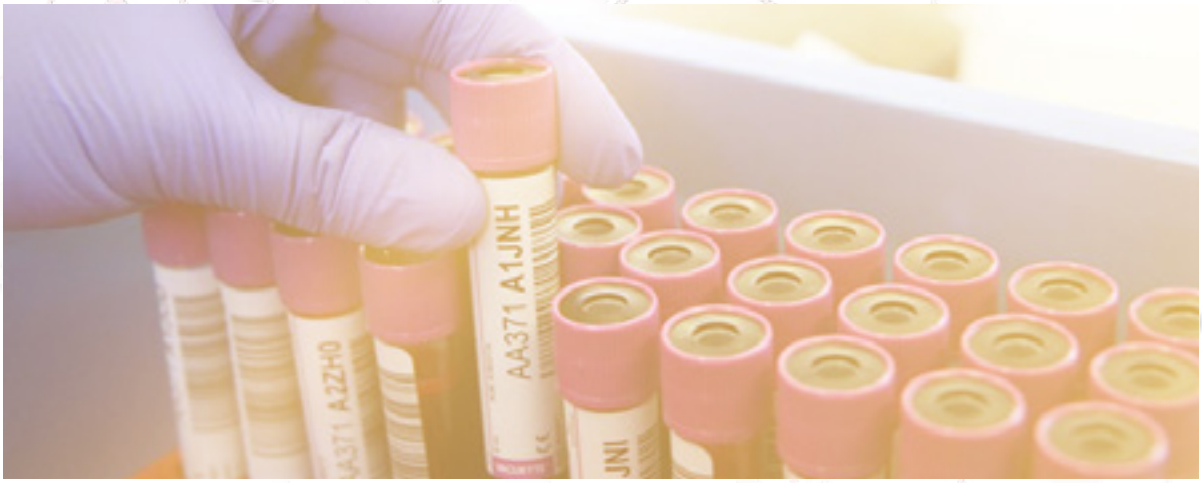
The need for consistent pan-European Directives: the next legal framework should draw on the existing Directives but also consider dynamic recent scientific and technical achievements, epidemiological changes, and differences between Member States. At present, epidemiological and other local factors cannot be taken into account when making decisions on the implementation of the Directives.

Thus, the revised Directives should reassert principles but not include technical guidelines. The Directives should rather refer to the EDQM Blood Guide and all blood components now supplied for various uses by BTCs should be taken into account and regularly revised by means of the EDQM Blood Guide.

This would allow quicker adaptation for donor deferrals, for instance, based on strict (actual) risks assessment and on new developing scientific evidence, as the Guide is revised every two years.

Guidelines and manuals such as those produced through the European Blood Inspection Projects and Joint Actions, e.g. EuBIS[8] and VISTART[9] should be the reference guide for any EU Blood Establishments and national competent authorities when assessing policies regarding quality, standard processes or operating procedures.

In practice, this means that donor eligibility and donor selection policies, such as deferrals for tattoo, body piercing, endoscopy etc. and other medical details should not be part of the new Directive.



[8]Quality management and inspection of Blood Establishments, EU project, https://www.eubis-europe.eu/
[9]Vigilance and inspection for the safety of transfusion assisted reproduction and transplantation EU Joint Action, https://vistart-ja.eu/about-vistart

6 The Need for Clarity and Coherence

Because of loose definitions, Member States have experienced challenges in maintaining compliance with the legislation, or with understanding the required resources for inspections.

The EU must include in the next set of EU BTC legislation clear definitions, including those for the roles and tasks of the European Centre for Disease Prevention and Control (ECDC), as a key agency and reference point for any epidemiologically based interventions, and EDQM.

Nowadays, a number of blood components not used for transfusion but for other therapeutic purposes (e.g., serum eye drops; fibrin glue or platelet rich plasma) are not included in the scope of the Directive. For coherence, the scope of future BTC legislation must be clarified and extended to include these products.

Coherence between EU legislation is also a key element of the revision of the BTC Directives, when, in the past, serious adverse reactions (SAR) in donors, were defined in 2002/98/EC but not considered in Directive 2005/61/EC. SAR in recipients need to be further defined and a common approach agreed between Member States. As the science regarding SAR is evolving, this coherence is necessary and so is flexibility within the Directive to allow updates.

Need for consistent manufacturing standards: there is currently a lack of coherence with regard to manufacturing standards. For instance, those in Blood Directive e.g. Reference to Good Practice Guidelines, are not currently applied to procedures for tissues and cells.

Furthermore, EBA encourages the EU to support the efforts of Member States either to increase their resources to enhance security and quality, or to mutualise at regional levels the inspections tasks.

Some cross-reference between the relative legislative instruments such as the Blood Directives and the Medical Devices Regulation must be put in place to ensure that Good Manufacturing Practices are respected. Currently, when products from blood for topical/non transfusion use (such as platelet-rich plasma in surgical setting) are produced in a hospital setting, they are not covered by the Blood Directives. Medical Devices Regulation can only guarantee the safety of the device used to produce the product, but not the quality and safety of the blood product itself.

EBA calls on the EU to act

EBA calls on the EU to adopt measures to meet the needs of European patients: while respecting ethical matters pertaining to BTC donations, donor's health protection, coherence between various EU legislation concerning the sector, EBA calls on the EU Commission, Parliament and Council, to:

- ***Table*** and adopt measures for BTC, to ensure that the needs of European patients are met.
- ***Provide*** regular updates: Regularly updating guidelines will also ensure that technical and medical advancements are taken into consideration.
- ***Ensure*** European self-sufficiency: The EU must put in place measures that will support EU Member States reach self-sufficiency on blood and blood components, including plasma for fractionation, based on the principle of voluntary non-remunerated donation.
- ***Ensure*** that other EU legislations pertaining to blood and its components, such as the Pharmaceutical and Medical Devices Directives and Regulations support better access for patients to blood-based therapies, avoiding wastage, or increased costs incurred by additional administrative processes.

Together, Blood Establishments members of EBA*

16 million

Provide about 16 million units of blood and blood components to patients across the European Union, EFTA/EEA, UK

400 million

Serving a population of 400 million

8.5 million

Thanks to over 8.5 million donors

20.000 staff

And more than 20,000 staff

1 million mobile collections

800 donation centres

Through more than 800 donation centres and 1 million mobile collections

SAVING MILLIONS OF LIVES

**source: EBA internal survey of its members, April 2021*

Members of EBA

- **Austria**
- **Belgium**
  (French speaking and
  Red Cross Flanders)
- **Croatia**
- **Denmark**
- **Estonia**
- **Finland**
- **France**
- **Germany**
- **Greece**
- **Hungary**
- **Iceland**
- **Italy**
- **Latvia**
- **Lithuania**
- **Luxembourg**
- **Malta**
- **Netherlands**
- **Norway**
- **Portugal**
- **Slovenia**
- **Spain**
- **Sweden**
- **Switzerland**
- **United Kingdom:**
  Wales, England, Scotland,
  Northern Ireland

Observers: Serbia, ABC USA, North Macedonia

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Drafted by the EBA EU Directives Working Group, with EBA Secretariat

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