

Plasma donation: new thinking to serve Europe's patients

Practices & approaches for countries



About this report



This report presents the case for expanding the availability of blood plasma for the production of plasma-derived medicinal products for patients in all European countries, by growing donations of plasma in each country.

It summarizes practices that decision makers in Europe's national health systems can consider to contribute to stable and safe access to plasma donations, that are needed to make plasma-derived medicines for patients who often need life-long treatment.

Various approaches of combined public-private plasma donation and collection systems are discussed. For countries that do not yet have public-private donation approaches, the practices described here can provide useful guidance for developing an action plan to build a national plasma donation system that involves local donor communities.

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Executive Summary

Toward new approaches to plasma donation

In the coming decade European countries will see an increased need for plasma-derived medicines to treat their patients for a range of rare diseases and critical medical conditions. While demand for blood components for transfusion remains relatively stable, a European Commission survey (2014) shows that demand for plasma derivatives is increasing by some 6% per year.

PER PATIENT PER YEAR:

MORE THAN
1200:  Plasma donations to treat ONE PATIENT for HAEMOPHILIA.

MORE THAN
900:  Plasma donations to treat ONE ALPHA-1 PATIENT.

MORE THAN
130:  Plasma donations to treat ONE PATIENT with a PRIMARY IMMUNE DEFICIENCY.

The patient population that these plasma-derived medicines can treat has been growing steadily in recent years for four reasons: more people are being diagnosed with conditions thanks to the increased precision of medical diagnostics; more are being diagnosed early; people benefiting from these treatments are living longer; and there is more clinical evidence of these therapies' benefits for patients.

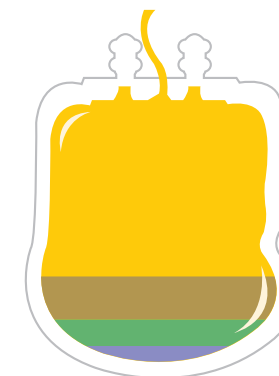
To meet this anticipated increase in need for plasma-derived medicines, and the donated plasma needed to produce them, health sector policy makers will need to put strategies in place to ensure a safe and stable supply of this blood component.

Additionally, new developments on the public health landscape, and unpredictable events such as COVID-19, highlight a need for countries to put in place private plasma donation approaches, that will help provide stable access to plasma-derived medicines to their citizens over the long term.

Plasma in Europe today is provided by a combination of nationally collected and imported donations. Some 3% of plasma used is given by volunteer donors in the US who are compensated for their efforts*.

*This figure excludes UK volumes.

PLASMA PROTEINS AND THE DISEASES THEY TREAT



- **Albumin (25 grams*)**
Shock, Burns, Major Surgeries, certain chronic liver diseases.
- **IVIG (Intravenous Immunoglobulin) (4 grams*)**
Primary Immunodeficiency Diseases, Autoimmune Diseases, Chronic Inflammatory Demyelinating Polyneuropathy, immune thrombocytopenia
- **Alpha-1 Antitrypsin (.15 to .30 grams*)**
Alpha-1 Antitrypsin Deficiency (Genetic COPD)
- **Coagulation Factors (Factor VIII: 300 to 450 IUs, Factor IX: 180 to 200 IUs*)**
Haemophilia A & B, von Willebrand Disease, other rare bleeding disorders

* Plasma Protein Yields per Liter of Plasma

Looking to the decades ahead, imported plasma will continue to be an important contribution to plasma-derived medicines produced for European patients. But as patients' needs and populations grow, countries can consider new thinking on how more locally donated plasma can be collected in their public systems to contribute to sustainable plasma supply in Europe.

Today's European plasma donation landscape

Some 38% of the plasma used in Europe today to treat patients is imported from the US.*

*This figure does not include UK volumes.

Today Europe has some 150 plasma private plasma donation centres (2020); around US has 900.

Some 44% of all directly donated plasma in Europe is given by donors in only four countries: Austria, Czech Republic, Germany and Hungary, who mainly use plasmapheresis.

Plasma is fundamentally different from blood

Plasma is a blood component. But it is unique and fundamentally different from blood in several ways. Some key facts:

- For many conditions that plasma-derived medicines treat, patients have no alternative treatments.
- Donating plasma takes longer than giving blood, but plasma donors can give larger volumes more frequently.
- The process for making medicines derived from human plasma is more complex and expensive than producing chemically synthesized medicines. It takes up to 7-12 months from donation to when a plasma-derived medicine is available. Some 57% of the cost of a plasma-derived medicine is in the manufacturing process; for other pharmaceutical medicines it is 14%.

Authorized frequency of plasma donation

When they donate blood, donors lose blood cells and plasma. Plasma donors lose only blood proteins. The differences in recovery periods for people in these two donation processes is the basis for national regulators

to allow donation of higher plasma volumes at a higher frequency than for whole blood. In Europe donors can give 650-850ml of plasma per donation. National rules on frequency of donation vary widely – between 20 and 60 times yearly.

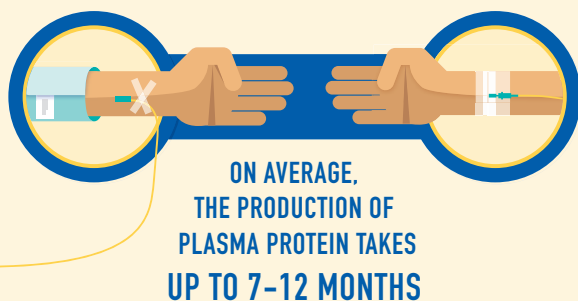
Combined public-private plasma donation

New approaches to plasma donation focus on moving from a public plasma donation system to a combined public-private donation network. In this model, donations to established national blood bank services are complemented by plasma given directly in a network of private donation centres. In some countries, such as Germany, all centres are private.

There are different variations on this model. The public-private plasma donation networks operating in Austria, Czech Republic, Germany and Hungary for the past decade provide excellent examples of how the public sector blood system can coexist with private sector plasmapheresis donation services to collect more plasma per capita.

How long does plasma protein production take?

The process to manufacture plasma protein therapies is lengthy because several complex steps must be taken to ensure products are safe and effective.



Will opening more plasma donation centres reduce whole blood donations in a country?

There is no empirical evidence to support the idea that plasma donations have a negative influence on traditional blood supplies in a country. Data from European countries that have opened private plasma donation centres show an opposite trend – when plasma donations increase, blood donations also increase.

A recent study of the evolution of the Czech Republic’s combined public-private donation system shows that blood collection volumes and frequency have remained stable as private

plasma donation has grown. There have been no decreases in the blood donation figures, despite the opening of ten plasma donation centres between 2007 and 2010. During this period, volumes of whole blood collection remained stable, as private plasma donation increased significantly.

Donations evolved nearly tenfold – from 6.8 liters per 1000 people in 2006 to 50 liters per 1000 people in 2010.

Austria, Germany and Hungary report that their combined plasma donation systems show similar results to their Czech counterparts over a ten-year period. Health professionals in these countries found that compensating donors for their effort and inconvenience is a determining factor in their ability to increase and sustain stable volumes of locally donated plasma.






Building long-term relationships with plasma donors

Potential donors across Europe generally do not know about the vital contribution that plasma makes to society and to transforming patients’ lives. This situation is complicated by the low public awareness of the possibility to donate plasma and of the difference between blood

and plasma. These are reasons why the level of plasma donations in Europe is below its potential. More effective donation can be achieved by including countries who are not currently pursuing private donation programmes.

Compensation

In their policies and regulations all European countries align with the principles of voluntary unpaid donation of blood and blood components, as set out in the European Commission’s report on the topic.⁵ At the same time they allow donors to be compensated for the costs they incur, recognising the considerable effort and inconvenience of donating plasma.

 Austria	Up to 50 times yearly
 Belgium	Every 2 weeks, no more than 23 times yearly
 Czech Republic	One donation every 2 weeks
 Germany	Up to 60 times yearly
 Hungary	Maximum 33 donations yearly, and one whole blood donation per year before giving plasma

While countries have different approaches, all are aligned with the principles of voluntary unpaid donation. For example, the system in **Czech Republic and Germany, is based on a fixed allowance**. Others reimburse specific expenses. Depending on what is authorized in national legislation, donors can give between 20-60 times yearly

Incentives for plasma donors in Europe

The report shows that 24 countries provide some form of incentive to donors of plasma and blood platelets: Austria, Belgium, Croatia, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Ireland, Italy, Latvia, Lithuania, Luxembourg, the Netherlands, Norway, Malta, Poland, Romania, Spain, Slovenia, Sweden, and the United Kingdom.

Incentives include:

- Reimbursement of medical costs
- Compensation linked to loss of earnings
- Small tax deduction for costs incurred
- Free physical check-up
- Food vouchers
- Time off work
- Reimbursement of travel costs
- Small tokens
- Refreshments

Rethinking countries' plasma self-sufficiency

The goal of attaining national plasma self-sufficiency is specified in global health forums and policies (EU, WHO) and in a number of European countries national health strategies.

If national health authorities' ultimate goal is to secure stable access to plasma-derived medicines for their patients, it may be useful to reframe the concept of self-sufficiency around an access approach.

This would include practices such as increasing networks in countries for private plasma donation (plasmapheresis). This can be linked to Plasma-for-Product agreements with medicines producers for efficient medicines supply; and to contract fractionation – where plasma production resources can be shared among countries who do not have this infrastructure, or the scale to invest in it.

COVID 19 & pandemics: a changing situation for plasma donation

The efficacy of plasma and its derived medicines as a treatment for COVID-19 have not been conclusive, except for treatment at the very early stages. But the pandemic has raised interest in the potential of convalescent plasma to treat other viruses.

The experience of the pandemic, coupled with the effectiveness of plasma in treating diseases such as Ebola, has heightened the perception that plasma can be considered to help manage future outbreaks – creating more interest in securing a national plasma supply.

This shift in thinking may affect the global landscape for plasma donation in the medium term, suggesting that countries will need strategies to secure more donations in their pandemic preparedness plans.

1. New thinking on plasma donation for European countries

This report is intended as a resource to open a conversation with public health decision makers.

It discusses new approaches and offers examples of how countries can build on current plasma donation structures; to increase the donations which are needed to produce plasma-derived medicines for patients that need them.

European countries' challenge of increasing plasma donations to improve patient access

Attaining stable and safe access to human plasma from European donors to produce critical medicines for European patients is a goal voiced by most countries' health services.

This view has long been supported by inter-governmental recommendations of the WHO and European Union¹, whose calls for more national autonomy for donation in plasma and other blood components date back several decades. These bodies recommend the donation of whole blood and plasma on a 'voluntary unpaid donation' basis.

European countries currently have a deficit in the plasma they need to produce medicines that meet their patients' needs. Today, plasma comes from a combination of in-country and imported donations. Some 38% of this life-giving material used in Europe to make plasma-derived medicines, is given by donors in the US who are compensated. In Europe today, most countries follow the principle of Voluntary Unpaid Donations, where donors can receive reimbursement for expenses incurred or a fixed allowance that recognises the inconvenience of donating plasma.

Austria, Czech Republic, Germany and Hungary have policies that authorize different types of compensation to donors who give in private plasma donation centres.

Looking to the decades ahead, imported plasma will continue to make an important contribution needed to make plasma-derived medicines that improve the quality of life for an increasing number of patients in every European country.

But countries will also benefit from cooperating on new approaches to plasma donation. For example, in an ecosystem that offers diversified donations of plasma by growing communities of donors in all European countries.

Europe's decision makers are faced with an evolving public health landscape. There is a growing population of patients that can benefit from plasma-derived medicines. Medical research is identifying new indications that plasma can control and cure. Likewise, more precise diagnoses mean that more existing plasma-treatable conditions are being identified.



For public health decision makers, this challenge can be summarized in three imperatives:

- **Achieving improved access to plasma-derived medicines**, by building more plasmapheresis programmes across Europe.
- Doing this in a way that guarantees the **highest levels of safety for donors** and the plasma materials they give.
- **Reconciling the 'public goods' character of plasma donation**, with accepted standards for voluntary unpaid donations – by recognising and thanking plasma donors for their commitment and efforts they make to give plasma frequently.

New approaches that countries can consider to ensure more plasma donations

The good news is that there are useful examples from several European countries today. They show how the public sector blood system can work together with private sector plasmapheresis plasma donation services to increase donations at country level.

These models respect the principle of voluntary unpaid donation in national policies. They allow donors to be recognised for the costs they incur, and the considerable effort and inconvenience of donating plasma. Many plasma donors give on average 20 times yearly, and up to 50-60 times.

Toward a regional/global plasma ecosystem

Plasma is a critical source material of human origin and a global needed to make specialised plasma-derived medicines that will be needed by millions more people in the coming decade. New thinking on policies and practices for plasma donation has the potential to link countries in a regional and global ecosystem for plasma donation, exchange and the sharing of related know-how.


European countries have different options to build systems for safe and stable plasma donations. Options include fully public systems; and combined public-private plasma donation networks.

There is no single pathway; all variations of plasma donation and processing are needed.

The guiding principle is that plasma donors are protected by the highest safety standards; and patients benefit from a public health system that ensures stable access to high-quality plasma to produce safe and efficacious plasma-derived therapies – in line with national health policies and ethical and cultural norms.



2. Europe's evolving plasma donation landscape



Significant volumes of the blood plasma that is needed to make the plasma-derived medicines used every day by European patients is imported from outside the European Union.

To secure this critical resource for European patients, countries have the potential to encourage a higher volume of plasma donations from their donor communities.

Today several European countries have put in place innovative approaches that show how this is possible.

The evolving plasma donation landscape

In an effort to increase their donations of plasma, some European countries have put in place new systems. They complement existing public whole blood and plasma donation infrastructure by adding a network of private plasma donation centres.

Austria, Czech Republic, Germany and Hungary now run a combined public and private sector approach for plasma donation. Here, private plasma donation centres work alongside the traditional blood donation system, bringing plasma donations from new donor communities. This dual approach typically provides three times more plasma per resident compared with other countries in Europe.^{2,3,4}

A critical aspect of effective plasma donation is the lasting relationships that are needed with new plasma donors. These four countries' blood/plasma policies allow plasma donation centres to offer lump sum compensation or allowance to donors for their participation. Some 24 European countries currently offer plasma donors non-monetary compensation for their efforts – recognising that giving plasma is an inconvenience compared with giving.⁵

Will the growth of new private plasma donation centres reduce whole blood donations to the public system?

As countries consider moving to a public-private sector plasma donation model, some public health officials have voiced concerns that these new entries will disrupt the established blood donation system. They feel that new private sector plasma networks can potentially turn away traditional blood donors, with an overall negative effect on the blood collection sector.

Analysis of data from a decade of combined blood-plasma donation approaches shows no evidence that compensation-based plasma donations from private centres affects established whole blood donations.



Some 38% of the plasma used in Europe today for medicines production is imported from the US.*

*This figure does not include UK volumes.

Today Europe has 160 private plasma donation centres (2020); the US has around 900.^{2,3,4}

Some 44% of all directly donated plasma in Europe is given by donors in Austria, Czech Republic, Germany and Hungary, who mainly use plasmapheresis.^{2,3,4}

Over the past decade Austria, Czech Republic, Germany and Hungary have reshaped their plasma donation systems to boost donations by opening networks of private plasma donation centres.

Stable blood and plasma donation volumes – example of the Czech Republic’s combined system

A recent study of the evolution of the Czech Republic’s combined public-private plasma donation system shows that blood collection volumes and frequency have remained stable as plasma donations to private centres have grown.

There have been no decreases in the blood donation figures, despite the opening of ten plasma donation centres between 2007 and 2010. During this period, volumes of whole blood collection remained stable, as compensated plasma donation increased significantly. Donations evolved from 6.8 liters collected per 1000 inhabitants in 2006 to 50 per 1000 inhabitants in 2010.^{6,7}

Austria, Germany and Hungary report that their combined plasma donation systems show similar results to their Czech counterparts over a ten-year period. Health professionals in these countries have found that a determining factor in the ability to increase and sustain stable volumes of locally-donated plasma was the fact that donors are compensated with an allowance.



Cross-border donations

Cross-border donation of blood and blood products is happening in some EU regions. Czech Republic, Estonia, Luxembourg, Poland, Sweden and Norway have policies or guidelines for cross-border donation.

While compensation is not a determining factor, these incentives help build lasting relationships with donors – a critical aspect of building a stable plasma donor network. As part of its policy, to avoid competition between the established blood donation system and the more recent practice of giving plasma, Hungary requires every plasma donor to give blood once yearly, uncompensated.⁸

What policies for national self-sufficiency?

Some 22 countries have policies for self-sufficiency in blood and blood components:

Austria, Belgium, Bulgaria, Croatia Czech Republic, Cyprus, Denmark, France, Germany, Greece, Hungary, Italy, Latvia, Lithuania, Malta, Norway Poland, Portugal, Romania, Spain, Slovenia and Sweden, Spain, Slovenia and Sweden.

Of these countries, only 13 have explicitly defined the concept of self-sufficiency:

Austria, Bulgaria, Czech Republic, Cyprus, France, Hungary, Italy, Malta, Portugal, Romania, Spain, Sweden and Croatia.

France, Greece, Luxembourg, Malta, Slovakia and Norway **have bilateral agreements or cooperation structures** to ensure appropriate supply of blood and blood components to their country.

3. About plasma & plasma protein therapies



Some 300,000 European patients rely on plasma protein therapies every day to treat a range of critical medical conditions.

These include rare, often genetic, diseases and chronic conditions, or life-threatening medical situations resulting from accidents and trauma.

For these patients, plasma-derived medicines are a lifeline, helping the body replace missing or deficient proteins. Without stable access to these treatments, many will not survive or have will a severely reduced quality of life.

Plasma - key facts

Life-saving treatment for many critical conditions and rare diseases.

Plasma-derived medicines help patients living with a range of rare diseases that can only be treated by these therapies. They are also used in everyday medicine, emergency and critical care situations and in preventive medicine.

Over the past five decades, plasma-derived medicines have improved lives, and given a better quality of life to millions of people. The wide use of plasma-based immunoglobulin therapies, has increased survival rates of patients with common variable immune deficiency (CVID) without disease-related complications, from 30% in 1979 to almost normal life expectancy today.

Clotting factor medicines derived from plasma have significantly extended the life expectancy of patients with severe haemophilia A, from 19 years before 1955 to 71 years in 2001. These therapies consistently achieve significant clinical results against primary endpoints – for example, an 80% reduction in bleeds for haemophilia patients and over 65% reduction in infections for patients with immune deficiencies.⁹

PER PATIENT PER YEAR:

MORE THAN **1200:**  Plasma donations to treat ONE PATIENT for HAEMOPHILIA.

MORE THAN **900:**  Plasma donations to treat ONE ALPHA-1 PATIENT.

MORE THAN **130:**  Plasma donations to treat ONE PATIENT with a PRIMARY IMMUNE DEFICIENCY.

HOW PLASMA IS USED IN EVERYDAY MEDICINE



BURNS
(Albumin)



MAJOR SURGERY
(Albumin)



ORGAN TRANSPLANTS
(Anti-CMV IG)



LIVER CONDITIONS
(Albumin)



SHOCK
(Albumin)



RH INCOMPATIBILITY
Hemolytic disease of the new born



PAEDIATRIC HIV
Immune globulins



ANIMAL BITES
(Anti-Tetanus IG)



TRAUMA
(Albumin)



MAJOR CARDIAC SURGERIES
(Albumin)

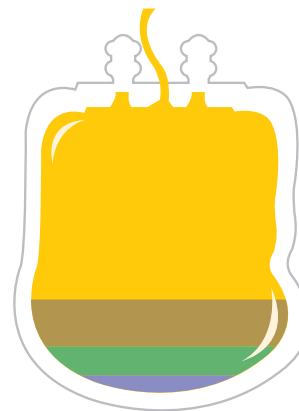


HEPATITIS
(Anti-HBV IG)



AUTO-IMMUNE DISEASES
(Immune globulins)

PLASMA PROTEINS AND THE DISEASES THEY TREAT

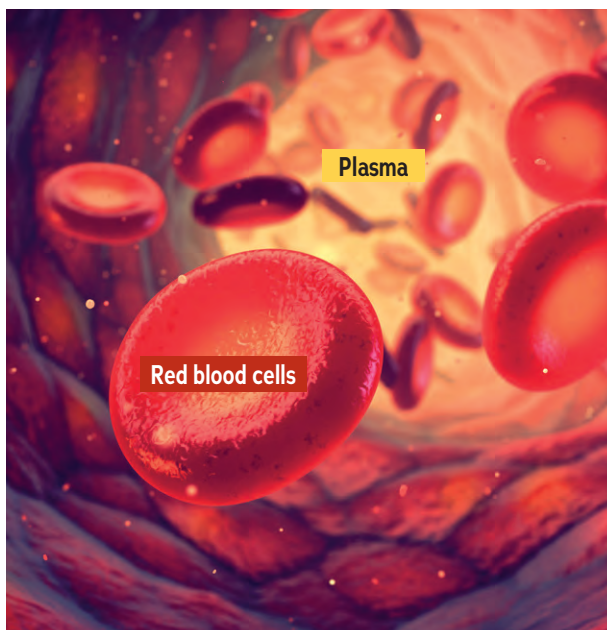


- **Albumin (25 grams*)**
Shock, Burns, Trauma, Liver conditions, Cardiopulmonary Bypass Surgery
- **IVIG (Intravenous Immunoglobulin) (4 grams*)**
Primary Immunodeficiencies, Secondary Antibody Deficiencies, Immune-mediated Neurological Diseases; Primary Thrombocytopenic Purpura; Other Autoimmune Diseases
- **Alpha-I Antitrypsin (.15 to .30 grams*)**
Alpha-I Antitrypsin Deficiency (Genetic COPD)
- **Coagulation Factors (Factor VIII: 300 to 450 IUs, Factor IX: 180 to 200 IUs*)**
Haemophilia A & B, von Willebrand Disease, other Bleeding Disorders

* Plasma Protein Yields per Liter of Plasma

What is plasma?

Plasma is the liquid part of human blood. Some 55% of blood is plasma, the remaining 45% is composed of red blood cells, white blood cells and platelets that are suspended in the plasma. Plasma is 92% water, it contains 7% of vital proteins such as albumin, globulins, coagulation factors, and 1% mineral salts, sugars, fats, hormones and vitamins.



Plasma has four vital functions in the human body:

- Maintaining blood pressure and volume.
- Supplying critical proteins for blood clotting and immunity.
- Carrying electrolytes such as sodium and potassium to our muscles.
- Helping maintain a proper pH balance in the body, which supports cell function.

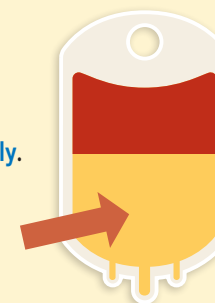
Plasma is:

- The single largest component of human blood, comprising about 55%, and contains water, salts, enzymes, antibodies.
- Composed of 92% water.
- A transport medium for cells and a variety of substances vital to the human body.
- Critical for a variety of functions in the body, including clotting blood, fighting diseases and other critical functions.

Plasma is the straw-coloured liquid portion of blood

comprised of water, salts, and proteins. 55% of the total blood volume is plasma. Due to its unique biological composition, it cannot be prepared synthetically.

55% OF TOTAL BLOOD VOLUME IS PLASMA



Plasma protein therapies are medicines made from donated plasma.

These therapies are used to treat a number of rare, chronic, conditions including primary immunodeficiencies, chronic inflammatory demyelinating polyneuropathy, hereditary angioedema, alpha-1 antitrypsin deficiency, and bleeding disorders such as haemophilia.



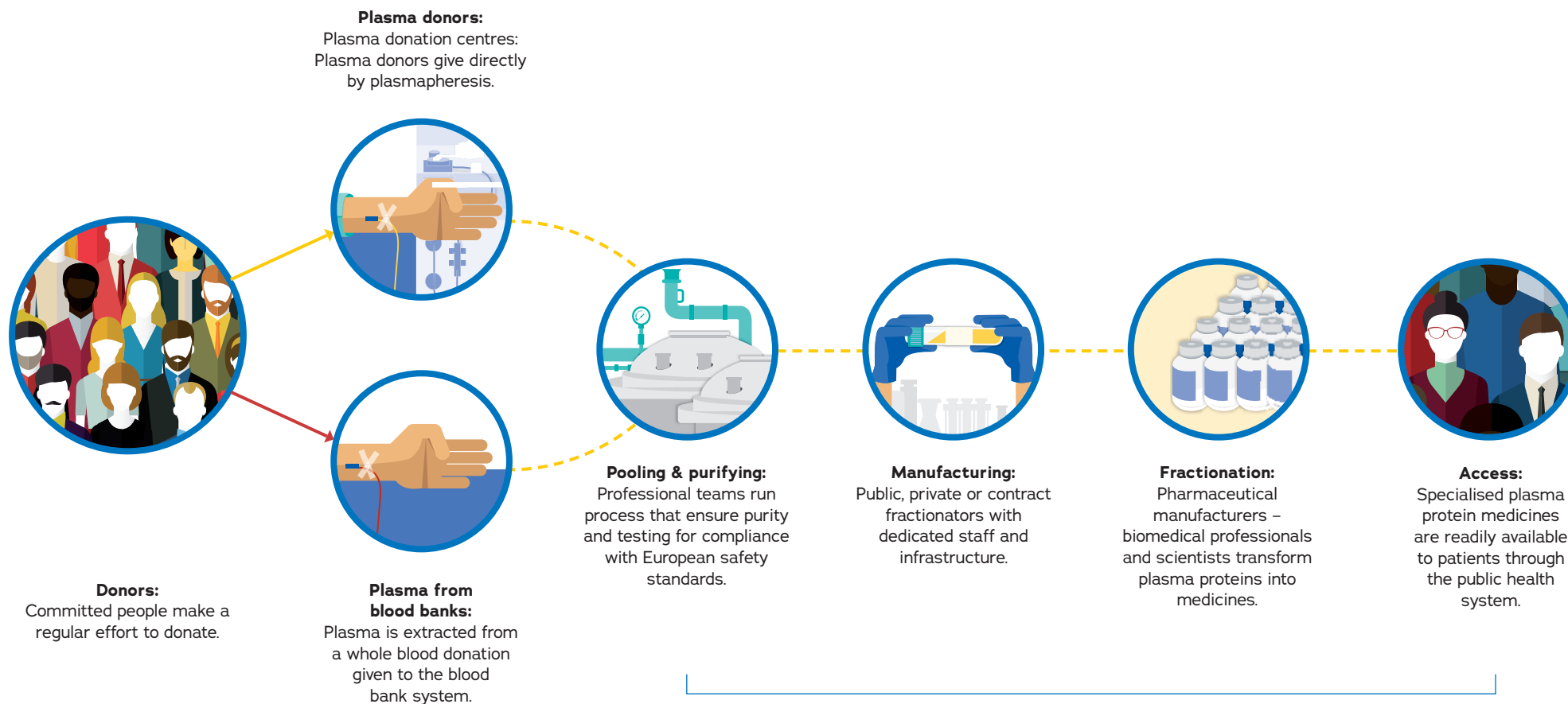
Plasma donation

Plasma is donated in two ways:

- Direct donation by plasmapheresis**, is a process, that removes plasma (source plasma) from the donor's blood and returns the remaining cellular components to them. This is done at a specialised plasma donation centre or blood centre. Donating plasma takes 45 minutes and can be done more frequently than blood donation, **20-60 times yearly**, depending on national legislation. One plasma donation gives 650-880ml.
- Separated from whole blood** through a whole blood donation at the national blood bank system. After donation blood is separated in its different components (recovered plasma). A whole blood donation takes about 10 minutes and can be done between **4-6 times per year** depending on gender). One whole blood donation of 500ml gives some 250-300ml of plasma.

	Extraction	Donation	Frequency	Duration	Volume
SOURCE PLASMA		<p>Plasma <i>plasmapheresis</i></p>	<p>1 x weekly</p>	<p>90 min</p>	<p>~820ml</p>
RECOVERED PLASMA		<p>Blood <i>blood donation</i></p>	<p>4-6 x yearly</p>	<p>30 min</p>	<p>~250ml</p>

The manufacturing process of plasma-derived medicines



ON AVERAGE, THE PRODUCTION OF PLASMA-DERIVED MEDICINES TAKES 7-12 MONTHS

Conditions treated by plasma-derived medicines

THERAPY	CONDITIONS TREATED	TREATMENT OUTCOMES
<p>Coagulation factors Essential for blood clotting need, used to treat genetic bleeding disorders and surgical bleeding.</p>	<ul style="list-style-type: none"> Bleeding from trauma Over-dosage of anticoagulants Liver disease <p>Bleeding disorders</p> <ul style="list-style-type: none"> Bleeding disorders of genetic origin with impaired clotting Haemophilia A & B – rare disorders Von Willebrand disease – the most common bleeding disorder 	<ul style="list-style-type: none"> Improved quality of life Increased life span
<p>Immunoglobulines Proteins inactivating infectious agents such as bacteria and viruses and regulating immune system function. Proteins protecting body from infections caused by viruses and bacteria and regulating immune system function.</p>	<p>Immunodeficiencies</p> <ul style="list-style-type: none"> Primary – Life-threatening genetic defect that compromises the immune system Secondary – Caused by infections, cancer treatments, certain medications <p>Auto-immune diseases Chronic Inflammatory Demyelinating Polyneuropathy (CIDP) A rare disorder of the peripheral nerves.</p> <p>Immune thrombocytopenia (ITP) A bleeding disorder in which the over-reactive immune system destroys platelets important for clot formation.</p>	<ul style="list-style-type: none"> Improved quality of life Increased life-expectancy Infection prevention
<p>Hyper-immune globulines Prevention and treatment of specific infections and medical conditions.</p>	<ul style="list-style-type: none"> Rabies, tetanus, hepatitis and other infections Rh negative pregnancy and hemolytic disease of the newborn 	<ul style="list-style-type: none"> Prevention Treatment Protection of babies in utero
<p>Alfa1-Protease Inhibitors Protecting lung tissue from damaging effect by enzymes of inflammatory cells.</p>	<p>Alfa1-Antitrypsin Deficiency Disorder caused by the genetic defect that results in liver disease and life-threatening lung damage.</p>	<ul style="list-style-type: none"> Improved quality of life Decreased mortality and morbidity Increased life span
<p>Albumin The major plasma protein, regulating blood volume and providing essential functions.</p>	<ul style="list-style-type: none"> Fluid therapy Major surgeries Severe live disease Severe infections Septic shock Severe burns 	<ul style="list-style-type: none"> Lifesaving in severe situations Decreased morbidity and mortality Increased life span
<p>C1-esterase Inhibitor</p>	<p>Hereditary angioedema</p>	<ul style="list-style-type: none"> Improved quality of life Decreased mortality

4. Plasma is different from blood



Blood plasma differs from whole blood. It is a liquid portion of blood that does not contain blood cells. Donating plasma is a more complex process than blood donation. Plasma donors can give more frequently and larger volumes.

Plasma-derived medicines treat many conditions for which no alternative treatments exist.

Plasma is different from blood

Plasma is a blood component. But it is unique and fundamentally different from blood in several ways:

Donating plasma takes longer than giving blood. Plasma can be donated directly through a process called plasmapheresis, where only the plasma is collected and the cellular components are given back to the donor. This process is longer than the time needed to give blood, but plasma can be given more frequently because the human body replenishes plasma more quickly.

Plasma protein therapies are unique medicines. The source plasma material for manufacturing these medicines is of human origin. For most of the conditions that these therapies treat, patients have no alternative treatment except for these plasma-derived medicines.

Direct donation of plasma (plasmapheresis), in dedicated plasma donation centres, is less prevalent in Europe than in North America. The US has some 900 dedicated plasma donation centres. There are currently 150 private sector plasma centres in the EU (2020), but this number is growing, as more public health systems enact policies to increase plasma giving to private centres in their countries.

Plasma donors are unique

Plasma is a unique source for producing life-saving biological medicines. Plasma donors are critical for supporting patients' health and in many cases their survival. To guarantee that patients have sustained access to plasma-derived medicines, long-term relationships are needed between plasma donation centre and donors.

Patients that take life-saving medicines made from plasma proteins require treatment throughout the year. To meet this need for 300,000 patients across Europe, and a wider group, such as trauma and accident victims, who benefit from these medicines, European countries rely on a committed community of plasma donors who agree to donate frequently, year-round.

Plasma can be separated from whole blood donation given to the public blood system or donated directly by people in a private plasma donation centre. Direct plasma donation – known as plasmapheresis – generates two to three times more plasma than when recovered from whole blood donation. The vast majority of plasma used to produce plasma protein therapies comes from directly donated plasma.



Do compensated plasma donations reduce the number of donors giving uncompensated blood donations?

Assessments of the decreases in blood donation have been found to be primarily due to Patient Blood Management.


There is no evidence to support the idea that plasma donations have a negative influence on traditional blood supplies in a country.

Data from several European countries that have opened private plasma donation centres show an opposite trend. When plasma donations increase in the private sector, they also increase in the public non-compensated sector.

The plasma donor's situation is very different from that of a blood donor:

- Giving whole blood takes 10 minutes; donors can donate 4-6 times yearly depending on gender
- Giving plasma through plasmapheresis takes 45 minutes; donation frequency varies between 20 to 60 times per year depending on national legislation.

5. Plasma-derived medicines are different from synthesized pharmaceuticals

A photograph showing a person in a blue shirt sitting in a chair, donating plasma. A large bag of orange plasma is visible in the foreground on the left. The background is blurred, showing other people in a donation center.

The unique value chain for these medicines always starts with a person's donation of plasma.

To ensure access for all patients to these life-saving plasma-derived medicines, public health authorities need to plan for stable access to plasma-derived therapies under all circumstances.

Producing plasma-derived medicines takes much longer than the process to make chemically-synthesized pharmaceutical medicines.

The unique character of plasma-derived medicines

Patient access in the plasma protein therapy value chain

The value chain for producing plasma-derived medicines is unique – it always starts with a person’s donation of plasma.

The process of making specialised medicines derived from plasma takes much longer to produce chemically-synthesized pharmaceutical medicines. It takes 7-12 months to manufacture plasma-derived medicines, from the moment the donation is made until it is ready to be given to a patient.

Ensuring adequate access and supply of these medicines also requires effective planning by public health authorities to ensure that patients have stable access to their therapies under all circumstances.

A spike in need for more chemically-synthesized pharmaceuticals – for example in response to a pandemic – can be easily managed in this production process. In contrast, the donor-to-patient plasma-derived medicine pathway needs to be planned months in advance. Obtaining large additional quantities of plasma to produce these medicines cannot be done overnight.

In planning for access to plasma-derived medicines, it is vital that sufficient plasma volumes from donors are always available.

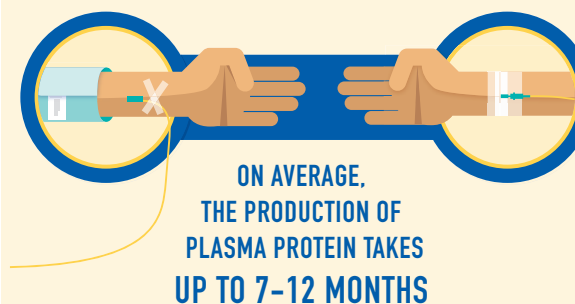
A plasma-derived medicine that is needed today has been a year in the making. This means that, in a crisis situation where large volumes of medicines are needed rapidly, a public plasma collection system may not have the flexibility to deliver more donated plasma needed for medicines production. A combined system where public and private plasma donation systems coexist – or with sharing of donated plasma across regions – will increase certainty for patients to have stable access to the treatments they need.

Unique and non-interchangeable medicines

Plasma-derived medicines cannot be used interchangeably to treat a patient with similar conditions, even in a same class of medicines. Each plasma protein therapy is unique due to differences in manufacturing processes, and because patients’ specific responses to the therapy will differ, depending on the person’s health situation.

How long does plasma protein production take?

The process to manufacture plasma protein therapies is lengthy because several complex steps must be taken to ensure products are safe and effective.



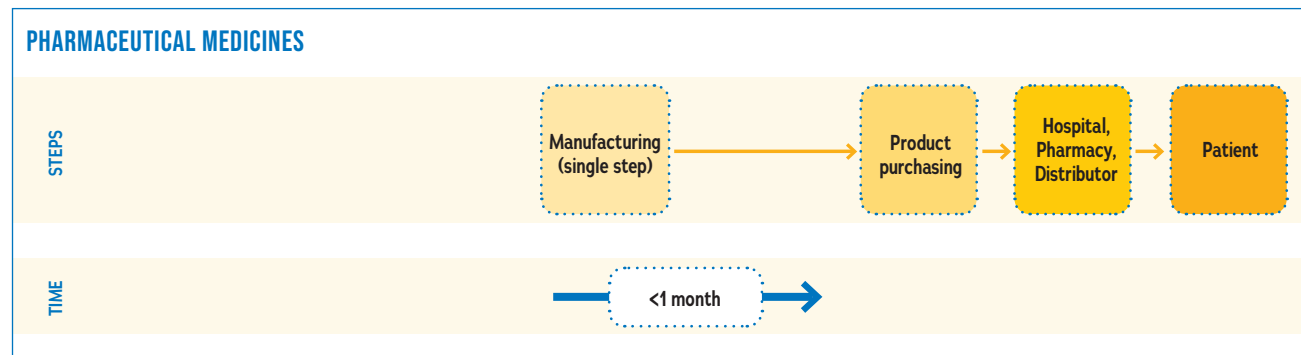
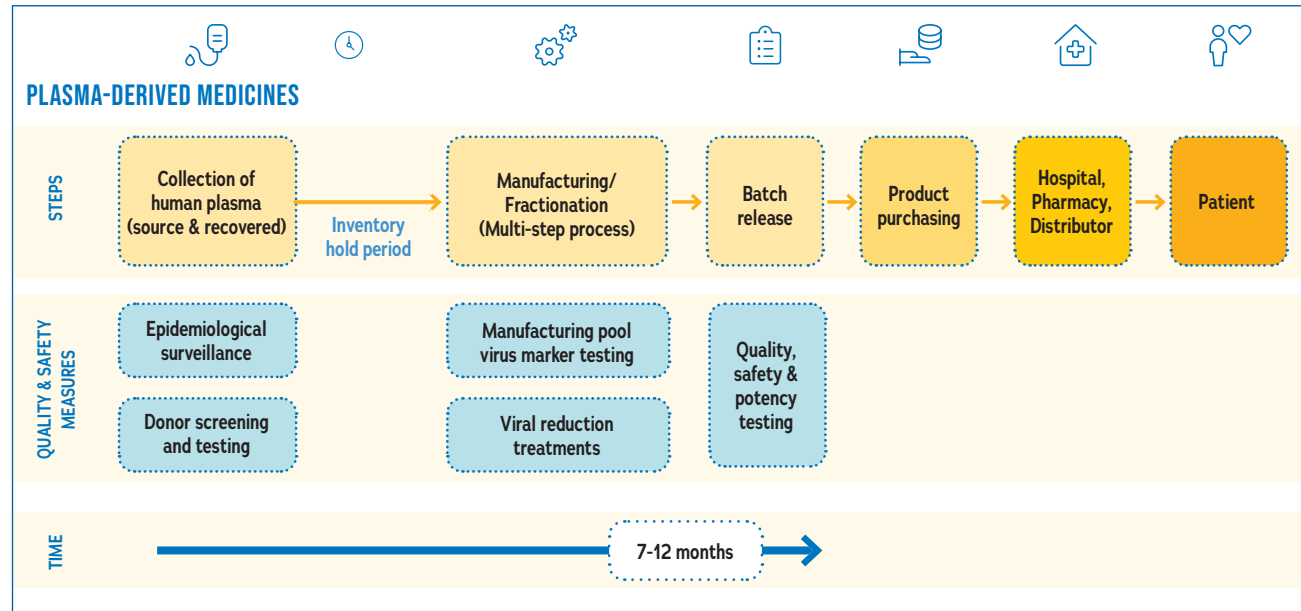
For example, a patient’s tolerance of the therapy may depend on the variation in the composition of components, the dosage and routes of administration. To identify optimal treatment for each patient, physicians do complex evaluations to identify the appropriate brand, dosage and administration route.

Co-morbidities will also indicate which brand therapy in a class of treatments is optimal for that patient.¹⁰



The donor-to-patient pathway is fundamentally different for the creation of plasma protein therapies than for chemically synthesized medicines.

- **The essential building block of plasma-derived medicines is human-donated plasma**, a material that cannot be re-created in a laboratory or by synthesis used in the process for making other pharmaceutical medicines.
- **The production process of medicines derived from human plasma is more complex** and expensive than chemically-synthesized medicines. It takes 7-12 months from donation before a plasma-derived medicine is available. Some 57% of the cost of a plasma-derived medicine is in the manufacturing process; for other pharmaceutical medicines it is 14%.
Source: Vintura; Grabowski and Manning 2018
- **Each medicine derived from plasma has its unique biochemical profile, and is not interchangeable with other treatments.** Medicines regulators specify them as treatments for which no generic or substitution treatments exist.



Source: Burnouf 2018, PPTA analysis, Vin 1

6. New plasma donation approaches in Europe



There is no single pathway for providing access to plasma-derived medicines.

Whatever the choice, the guiding principle is that patients benefit from a system that contributes to stable access to plasma-derived medicines to ensure their treatment, in-line with national health policies and accepted cultural norms.

Plasma donation approaches

Current donation practices in Europe

Plasma-derived medicines help patients living with a range of rare diseases that can only be treated by these therapies. They are also used in everyday medicine, emergency and critical care situations and in preventive medicine.

Most European countries authorize specific organisations to collect whole blood and plasma. For example, France and Finland have one approved national plasma collection body; Poland authorizes collection in state-certified public hospitals. The UK has recently reversed its decades-old ban on using plasma from the public blood system for medicines, making local production with plasma from UK blood donors possible again.¹¹

Several countries – Austria, Czech Republic, Germany and Hungary – have systems where public blood and plasma services coexist with private sector plasma donor centres. Depending on national regulations, a plasma donation centre that collects plasma from donors who use ‘plasmapheresis’ can be public, non-profit or private.

Plasma is obtained in two ways:

- **‘Direct’ donation in dedicated plasma centres** that use the ‘plasmapheresis’ process (**source plasma**). Here, the donor’s blood runs through a medical device that separates plasma from other blood cellular components, which are then returned to the donor.
- **Separated from whole blood donation made by people to the national blood bank system (recovered plasma)**. After donation, blood is separated into different components; plasma is one of these.

In both approaches, collected plasma is pooled, purified and specific proteins are separated in the ‘fractionation’ process. These proteins are then used by medicines producers in the plasma protein therapies that are prescribed to treat patients living with rare and debilitating conditions. In a nutshell, this is the pathway from plasma donor to patient.

	Extraction	Donation	Frequency	Duration	Volume
SOURCE PLASMA	<p>Donor Centre</p> <p>Blood → Plasma (direct plasma donation) → Used for making plasma-derived medicines</p> <p>Red cells</p>	<p>Plasma plasmapheresis</p>	<p>1 x weekly</p>	<p>90 min</p>	<p>~820ml</p>
RECOVERED PLASMA	<p>Donor Centre → Processing Centre</p> <p>Blood → Plasma (For hospital use (transfusion) + making plasma-derived medicines)</p> <p>Red cells (Hospital use)</p>	<p>Blood blood donation</p>	<p>4-6 x yearly</p>	<p>30 min</p>	<p>~250ml</p>

Creating public-private plasma donation partnerships that benefit patients and the public health system

How can countries best align the interests of public health services with private sector partners for the benefit of all patients that need plasma protein therapies?

This is a central question for public health decision makers as they explore strategies to secure plasma donations from a wider donor community.

The global picture of plasma-derived medicines points to a continually growing need for these therapies. Better diagnosis broadens the patient population that can benefit from them, and medical research is discovering new treatment areas. While demand for blood components for transfusion remains relatively stable, a European Commission survey (2014) shows that demand for plasma derivatives is increasing by some 6% per year.

To meet this need, medicines' producers will need more donated plasma to deliver the therapies that health services and patients need.

Plasma has a unique place in the medicines development landscape. It is a finite source material that cannot be made synthetically in a laboratory. It can only come from healthy, committed donors.

New approaches to ensuring national plasma donations call for partnerships between the public health system, medicines producers and patient organisations – all focused on delivering to patients' optimal access to the plasma-derived medicines that need.¹²

Novel plasma donation policies are in place in several European countries

Current public-private plasma donation approaches brokered by public authorities specify:

- A requirement for private sector partners that establish plasma donation centres to provide the health service with access to a specified volume of plasma-derived medicines at an agreed price, in return for authorization to operate.
- Access to pooled plasma for local medicines producers at an agreed cost.
- Agreement on the volume of plasma to remain in the country for national medicines production.
- Transfer of technology and know-how to the local medicines industry.

Country cases – the combined public/private approach

	AUSTRIA	CZECH REPUBLIC	GERMANY	HUNGARY
Population	8.8 million	11 million	83 million	10 million
Approach	Combined system: Austrian Red Cross collects plasma from whole blood donations; direct plasma donation (using plasmapheresis) by Red Cross and private sector plasma donation centres.	Combined system: Public blood/plasma system from whole blood donations; direct plasma donation at private sector plasma donation centres.	The German system has three pillars, active in both whole blood and plasmapheresis donation: Red Cross collection centres; municipal and hospital centres; private donation centres.	Combined system: National blood/plasma system from whole blood donations; direct plasma donation at private sector plasma donation centres.
Public plasma system	Whole blood collection for transfusions is exclusively public; by Red Cross and national hospitals. A small amount of plasma collection is public.	Public system for blood collection – reserved to blood banks and hospitals.	Whole blood and plasma collection: centres established at city, communal level and in hospitals and by the Red Cross.	Government-run whole blood collection.
Direct plasma donation (using plasmapheresis)	Plasma donors give in dedicated donation centres; owned by mix of international and national companies.	Plasma donors give in dedicated donation centres; owned by mix of international and national companies.	Plasma donors give in dedicated donation centres; owned by mix of international and national companies.	Plasma donors give in dedicated donation centres; owned by mix of international and national companies.
Direct plasma donation (using plasmapheresis)	20 centres nationwide	50 centres nationwide	80 centres nationwide Dedicated donation centres in 11 Länder	35 centres nationwide
Legislation on donation frequency	<ul style="list-style-type: none"> – 50 plasmapheresis donations/year – 3 donations in a 2-week period – 2 donations in 7 days – 1 donation in 72 hours – Max 700 ml/donation (without coagulant) 	<ul style="list-style-type: none"> – Plasmapheresis donation not more than every 14 days – Max 650 ml/donation(without coagulant) – Not more than 1.5l /week/person – Total plasma donation/person/year: max 25l 	<ul style="list-style-type: none"> – 60 plasmapheresis donations in 12 months – 2-day interval between donations Between 650ml-850 ml per donation (Depending on donor weight) 	<ul style="list-style-type: none"> – 33 plasmapheresis donations in 12 months – 1 donation within 72 hours – Max 800ml per donation (including coagulant)
Total amount of plasma collected/ per annum	<ul style="list-style-type: none"> – 590,000 liters, in slight decline – 67 liters per 1000 inhabitants 	<ul style="list-style-type: none"> – 500,000 liters – 45 liters per 1000 inhabitants 	<ul style="list-style-type: none"> – 3.1 million liters per year – 36 liters per 1000 inhabitants 	<ul style="list-style-type: none"> – 600,000 liters per year – 60 liters per 1000 inhabitants
Incentives	Financial compensation implicitly allowed, but financial profit explicitly not allowed.	Financial compensation allowed, capped at €12 per donation to cover donor costs (linked to minimum wage and varies per year); can be deducted from personal income tax.	Financial compensation is allowed for every entity collecting blood or blood components.	Financial compensation allowed – capped at €10 per donation – linked to minimum wage and can vary per year.
Observations	Pragmatic blood donation law. Allows covering of donor expenses, and similar costs as part of 'voluntary unpaid compensation'. Advertising for plasma donation is allowed.		Pragmatic plasma donation law. Donors can be compensated for both whole blood and plasma donations.. Non-compensation also allowed. Plasma donation volumes in Germany are relatively flat (not growing). Advertising for blood/plasma collection is allowed (not for compensation).	This national framework is a good example of public/private collaboration to encourage stable donation of whole blood and plasma in sufficient quantities. Plasma donation law for private plasma centres requires each donor to also donate whole blood for transfusion once yearly, uncompensated.

Setting-up a plasma donation centre: key considerations

Putting in place or expanding a public plasma donation scheme requires investments in infrastructure and network-building activities to inform the public and attract a community of donors interested in giving frequently.

Infrastructure development requires detailed planning and forecasting to ensure that operating costs are covered. Whether the centre is a publicly-funded facility or privately-owned, its establishment is subject to strict laws and regulations that govern facilities that handle materials of human origin.

Public blood/plasma collection architecture

A public plasma collection can have a centralized or distributed architecture, depending on a country's public health strategy, its blood/plasma policies and regulations, and the investment climate.

A centralized plasma infrastructure is typically composed of one or several large-scale donation centres. Some European countries collect whole blood only, later separating plasma from blood.

In other countries public blood centres also offer plasma donation with plasmapheresis equipment, accommodating some 30 donors at a time. Creating larger-scale plasmapheresis centres is a major public sector investment project, of the order of 250 million euro, plus a staff of salaried medical and technical professionals.

The operational plan for this type of centre requires an effective strategy and business plan that ensures sufficient throughput and donation volumes to offset the investment over a 25-year period. France, Italy and some other European countries operate this type of infrastructure.

Typically, of plasma recovered from donated blood, 75% is used for manufacturing plasma-derived medicines, with the remaining 20-25% is used for direct transfusion.

Making plasma protein therapy medicines

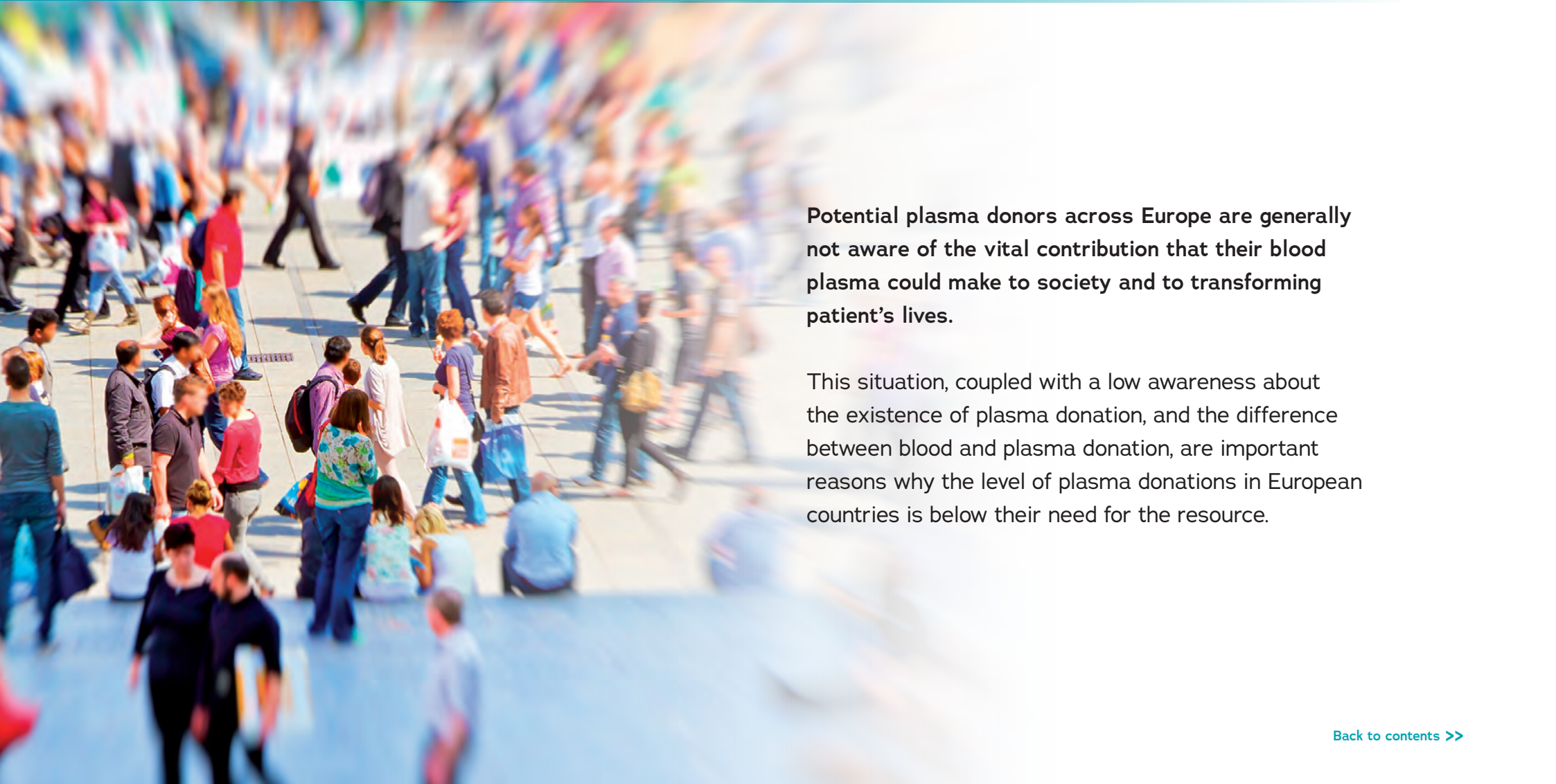
Depending on national regulations, dedicated plasma donation centres can be a part of the public health system, non-profit entities, or privately owned. In all cases they will be governed by health regulations for donor safety, product purity and compensation.

Producing a plasma protein therapy is a lengthy and complex process. It takes up to one year from the moment a donation is made until the therapy is ready for patients. Collected plasma is held in frozen storage for 60 days, pooled, and processed following a strict safety and purification regime.

It is then sent to a manufacturing facility that makes plasma-derived medicinal products. Here plasma is further tested; the manufacturing process uses fractionation to extract therapeutic proteins from the plasma. These protein fractions are further purified to extract proteins of interest, which are then cleared of potential viruses by additional steps.

The purified proteins are formulated into ready-to-use medicine, tested for sterility, packaged, labeled, and distributed through public health systems.

7. Building relationships for long-term plasma donation in countries



Potential plasma donors across Europe are generally not aware of the vital contribution that their blood plasma could make to society and to transforming patient's lives.

This situation, coupled with a low awareness about the existence of plasma donation, and the difference between blood and plasma donation, are important reasons why the level of plasma donations in European countries is below their need for the resource.

The donor's perspective

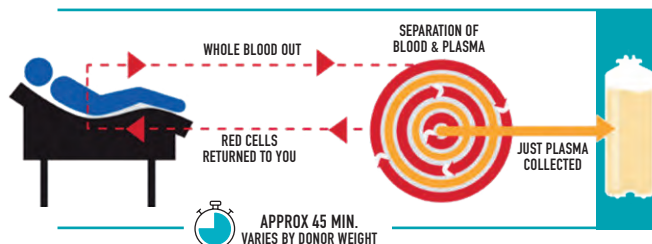
Plasma in the donor patient-relationship

The relationship between plasma donor and patient is central to the value that plasma brings to society through plasma-derived medicines.

Many potential donors are not aware that in addition to giving blood, they can donate plasma, which is used to make life-saving therapies that benefit thousands of people. A combined awareness effort between European and national health authorities the general public and patient groups will help inform and attract new donor communities to give plasma.

Many people that donate plasma feel that they contribute to saving lives. And many patients recognise that the source of their medicines comes from plasma given by another person.

Looking at these changes in plasma donation, industry experts commented that private investment injected into a public system – where dedicated plasma donation centres are private entities – can help boost the efficiency of plasma donation and the number of donation centres in a country. As part of a national



health policy, a shift to a public-private donation makes it easier for plasma donors to give – closer to home, for example. This also reduces cost pressure on the very high public investment levels needed to expand a current national donation network.

In designing a decentralized donation network, a key consideration in a country's plan is to understand what motivates plasma donors to give, and give regularly. Clarity on this will help build a lasting relationship with a wider donor community.

In assessing its new public-private plasma donation architecture, the Bavarian Red Cross observed that the profiles of its blood and plasma donors are somewhat different.

The typical blood donor tends to be older, giving twice yearly. In contrast, plasma donors give on average 20 times yearly.

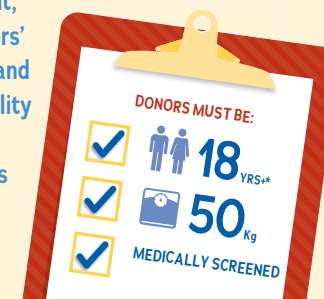
This frequency of donation requires a higher level of commitment and can explain why plasma donating may be more appealing to a younger population.

For policy makers designing their future plasma donation strategies, the success of the approach they choose will depend on knowing who their donors are and what factors motivate them to give frequently.¹³

Qualified donor programmes

The PPTA independent Qualified Donor programme requires all prospective donors giving for use by its partners to have two satisfactory health screenings and negative test results within six months, before being authorized to give plasma. Without meeting this requirement their plasma will not be used to manufacture plasma-derived medicines.

This policy is important, firstly to protect donors' health and wellbeing, and to help ensure the quality and safety of the therapies that patients need to treat life-threatening diseases.



Authorized frequency of plasma donation – some country examples

The effects blood and plasma donation on the human body are quite different. A blood donor's recovery period after giving whole blood brings a loss of blood cells and plasma.

In contrast, plasma donations cause only a loss of blood proteins. This difference is the basis for national health regulatory authorities to allow donation of higher plasma volumes at a higher frequency from plasma donors than from whole blood donors.

 Austria	Up to 50 times yearly
 Belgium	Every 2 weeks, no more than 20 times yearly
 Czech Republic	One donation every 2 weeks
 Germany	Up to 60 times yearly
 Hungary	Maximum 33 donations yearly, and one whole blood donation per year before giving plasma

In Europe donors can give 650-850ml of plasma per donation. Countries' rules on frequency of donation vary widely – between 20 and 60 times yearly. Austria allows 50 donations and Germany 60.¹⁴

The European studies, Safety of Intensive Plasmapheresis, assess plasma donor safety factors. Their data concludes that participating in plasmapheresis under intensified conditions is safe, even for first-time and inexperienced donors (see section: Health & Safety for Donors).




How much plasma do we really need?


EU countries currently have a deficit of 5.15 million liters of the plasma that is needed to manufacture life-saving plasma-derived medicinal products for their patients.


Considering that a plasma protein therapy treatment for one year for a person living with

Alpha-1 requires 900 donations, public health authorities interested in developing a stable donor community need to better understand what actions and incentives can help encourage sustained plasma donations. Finding ways to educate plasma donors about their direct impact on patients' lives will help create the lasting relationships that are needed to build a strong donor community.

PER PATIENT PER YEAR:

MORE THAN
1200: 
Plasma donations to treat
ONE PATIENT for HAEMOPHILIA.

MORE THAN
900: 
Plasma donations to treat
ONE ALPHA-1 PATIENT.

MORE THAN
130: 
Plasma donations to treat
ONE PATIENT with a PRIMARY IMMUNE DEFICIENCY.

8. Donor incentives & compensation



The specific nature of plasma donation requires a novel approach to donors. An effective plasma collection programme requires building long term relationships with donor communities.

Doing this requires providing potential donors with clear information about the positive impact a person can make on someone's life by giving plasma. This can be supported by incentives that recognise the substantial commitment and inconvenience that donors make when they donate plasma.

Today some 24 EU countries have schemes to cover costs incurred by plasma donors or compensate them for their effort and the inconvenience related to donating, following the principle of Voluntary Unpaid Donation (VUD).¹⁵

Compensation policies & practices

Donor compensation within voluntary unpaid donation guidelines

Plasma-derived medicines help patients living with a range of rare diseases that can only be treated by these therapies. They are also used in everyday medicine, emergency and critical care situations and in preventive medicine.

In their policies and regulations European countries always align with the principles of voluntary unpaid donation of blood and blood components, set out in the European Commission's report on the topic. It presents a comprehensive review of voluntary unpaid donation practices and policies across the region¹⁶.

At the same time, most countries have incentive schemes to recognise the effort and inconvenience people who donate plasma. In practice, 'compensation' to donors includes meal vouchers, days off work, reimbursement of transport costs, refreshments, fixed rate allowance and other benefits.

Tokens and in-kind compensation across Europe

A multi-country survey presented in the European Commission report on voluntary unpaid donations notes that it is common practice in most EU countries to give donors refreshments (25 + Lichtenstein and Norway); or small tokens such as pins, pens, towels, t-shirts and mugs (22 countries). Donors in half of EU countries reimburse donors for travel costs and give time off work in the public and private sectors.

Some 13 countries report guiding principles for compensating donors of blood and blood components. In general, principles are set out in national laws, decrees or non-binding recommendations, and define the type of compensation and other practices are allowed, and the circumstances.

Compensation values for donating blood and blood products are reported at €15-30 (Austria, Czech Republic, Germany, Latvia, Romania). In Bulgaria and Czech Republic, maximum values are defined as a percentage of the national minimum wage.

The reported maximum values of refreshments and small tokens range between €1-10. Food vouchers are offered in seven countries. Reported maximum values are €1.4-4.1. Romania sets a fixed value of €15 for food vouchers.

For travel cost reimbursement for donor to travel to and from the place of donation, some countries cover actual costs; offer a cost per kilometer traveled; a fixed maximum value for the reimbursement or lump sum, irrespective of the actual costs.

In most EU countries donors get time off work. This varies between one day or less; to the time needed for the donation; or two days off.

In reality, all these ways of compensating donors have a monetary value. Yet compensation as a direct allowance, to compensate for expenses and inconvenience, seems to be the most efficient approach to encourage more plasma donations.

Monetary compensation

Several countries reported practices which involve the transfer of money other than for reimbursement of travel or medical costs (Austria, Bulgaria, Czech Republic, Germany, Latvia, Lithuania, Netherlands, Poland, Sweden). They compensate loss of earnings or the inconvenience related to donation, or are fixed sums of money. Fixed sums are irrespective of the costs actually incurred by the donor for the donation.

In Austria, Bulgaria and Poland, the transfer of money is only allowed under certain circumstances, such as:

- In emergency cases (Austria, Bulgaria, €23 per donation)
- Donation of rare blood groups (Poland);
- Donation plasmapheresis and platelets (Austria); platelets (Bulgaria), €46 per liter of blood passed through the device), or of anti-D plasma (Poland)
- Donations for the production of vaccines, immunoglobulins, research and diagnostics (Bulgaria) – €40 per donation.



The patients' voice on compensation

The Platform for Plasma Protein Users is a group of seven European patient organisations, representing 80,000 known patients in Europe that are treated regularly with plasma protein therapies; and other people with related conditions, totaling an estimated population of 650,000 people.

This group feels that it is not realistic to rely solely on voluntary non-remunerated plasma donations to guarantee a stable supply of plasma protein therapy medicines for patients – a situation that could evolve into a major public health issue.

It sees no conflict in having plasma collected in a country from the whole blood collection system as well as from donors who are compensated to give at dedicated plasma donation centres.

Given that the majority of plasma-derived medicines distributed worldwide are based on plasma that is given by donors [outside Europe] who are remunerated to give plasma through plasmapheresis at 20-25€ per donation.

(Source: PLUS opinion summarized in '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. https://ec.europa.eu/health/sites/default/files/blood_tissues_organ/docs/20150408_cc_report_en.pdf).












Specific incentives for plasma donors in Europe

A report by the European Commission⁷ highlights 24 countries that provide some form of incentive to donors of plasma and blood platelets: Austria, Belgium, Croatia, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Ireland, Italy, Latvia, Lithuania, Luxembourg, the Netherlands, Norway, Malta, Poland, Romania, Spain, Slovenia, Sweden, and the United Kingdom. Incentives include:

- Reimbursement of medical costs
- Compensation for effort and inconvenience linked to loss of earnings
- Other forms of incentives
- Free physical check-up
- Food vouchers
- Time off work
- Reimbursement of travel costs
- Small tokens
- Refreshments

Fixed compensation not directly related to actual donation costs

In some countries, donors can receive a fixed compensation that is not directly related to actual costs incurred. Some examples:

-
-  **Belgium's** official documents on blood, platelets and plasma refer to voluntary unpaid donations. Donors employed in the public sector are allowed leave from work for the duration donation plus a maximum of two hours of travel.
 -  **Denmark's** policy specifies voluntary, non-remunerated donations. Regional authorities, which run the Danish public hospitals, give a small fee per donation to the local donor-association to cover administrative and publicity costs.
 -  **Estonia's** guiding principles mention the possibility of giving incentives to donors of blood and blood components.
 -  **Greece** says that giving donors small souvenirs, soft drinks and travel costs is compatible with its voluntary and unpaid blood donation rules.
 -  **Italy's** policy allows public and private sector employees the day off when they donate blood or plasma; donor associations receive specific payments per donation to cover administrative and publicity costs.
 -  **Latvia's** guiding principles cover incentives to donors of blood and blood components, and policies to promote self-sufficiency of blood and blood components.
 -  **Lithuania's** guidance covers similar incentives for donors. Depending on the volume donated, donors may receive a compensation of up to two days of average salary.
 -  **Finland** specifies travel expenses may be reimbursed to the donor, within its voluntary and unpaid framework.
 -  **The Netherlands** specifies that plasma is to be given by voluntary donors, who may receive compensation which will not be beyond a reasonable cost of expenses incurred.
 -  **Poland's** blood and plasma donors are offered a recovery meal and can make a modest tax deduction and in some cases two days off work.
 -  **Slovakia's** incentive policy is enacted by each city; employers may recognise their employees' efforts with a financial bonus or a holiday allowance.
-

Guidelines for country plasma donor compensation policies

Oviedo Convention:

Principle of 'prohibition of financial gain...'

In considering the creation of a national policy to govern blood plasma donation and use – specifically issues of donor compensation – the Convention on Human Rights and Biomedicine (Oviedo Convention) offers guidance¹⁷. It sets out the principle of prohibition of financial gain with respect to human body and its parts from living or deceased donors.

The Council of Europe's guide to implementing of the principle provides a useful summary and definitions on 'compensation' and 'reimbursement' in the context of voluntary unpaid donations.

The principle states,

'...the human body and its parts shall not give rise to financial gain'.

According to the guide, this does not prevent compensation of donors for loss of earnings, and reimbursement of any other justifiable expenses. It states that the donation should be financially neutral for the donor, and that rules prohibiting financial gain do not hinder covering of a justifiable fee for medical or related technical services in connection with the donation.

The Convention:

Key points for plasma compensation

- States that reimbursement of expenses incurred and compensation for effort made and inconvenience is acceptable¹⁸, similar to the report: Human bodies: donation for medicine and research of the Nuffield Council on Bioethics (2012).¹⁹
- Calls for financial neutrality for the donor. This permits direct reimbursement and compensation of costs related to a donation, distinguishing between 'reimbursement' – expenses such as travel and related costs; and 'compensation' – that can be in the form of an allowance.²⁰
- States that where fixed-rate compensation is applied, its implementation must be specified in national law, with an upper limit for compensation. If an upper limit is not in the law, it should be set by an independent body created by national law²¹; and the scheme must not be an inducement to donate.²²
- Calls for measures to minimize the risk of harm to donors resulting from donation, such as national registers or traceability systems to limit how frequently a person can donate.²³

The case for 'reasonable proportional monetary compensation or allowance for donors' expenses and inconvenience: lessons from the from the European Blood, Cells & Tissues Directive

The EU Directive on Tissues and Cells, offers useful lessons that can be applied to compensation for plasma donations. The Tissues Directive leaves countries to define conditions for compensation, saying that 'donors may receive compensation, which is strictly limited to making good the expenses and inconveniences related to the donation'.

It notes that the degree of inconvenience and the effort required for different types of donations differ considerably – for example oocyte cell donors are compensated with sums of €1,000 or more, where sperm donors are compensated at far lower amounts in most European countries; the UK Human

Fertilization and Embryology Authority defines expense limits of £35 for sperm donors and £750 for egg donors, per donation. In contrast, the Blood Directive does not include this type of provision.

In practice, donors in some European countries are compensated with tax benefits, paid days off work in the public sector or even monetarily for donating – for example in Austria, Czech Republic, Germany and Hungary. It will be useful that these types of reasonable proportional monetary compensation for donors' expenses and inconvenience are recognised. This will help countries secure more plasma donations for the benefit of their patients..²⁴

Examples: compensation policies

Compensation policy of a donation centre in Czech Republic

Financial compensation

Request a refund for your costs and you will receive CZK 700 for one subscription *.
You can get up to CZK 1,400 a month.

* On the first visit, you will receive a refund of CZK 400 for one collection.
On the second visit, you will receive a refund of CZK 1,000 for one collection.
On subsequent visits, you will always receive a refund of CZK 700 for one collection.

Loyalty programme

With regular plasma donations, you collect points for the loyalty programme. You can choose one of our practical gifts.

Tax relief

Instead of direct financial compensation, you can opt to reduce your tax base by up to CZK 3,000 for each collection as part of a non-contributory donation.

Paid day off

After subscription from us, you will receive a confirmation of the subscription for your employer. By law, you are entitled to a day of paid leave.

Health overview

Regular donations will allow you to have a good overview of your health. We will test you for selected infectious diseases and

you will be able to consult with an expert on a regular medical examination.

Lunch Voucher

Lunch to a restaurant near the donor centre with a voucher worth CZK 200.

Compensation policy of a donation centre in Czech Republic

Financial compensation for donations

For each successful subscription, you will be paid a refund of CZK 700, and for the first subscription, an additional CZK 200 as compensation for registration.

* Donations can be made once every 14 days. The donation is governed by the provisions of §32 paragraph 2 of Act 373/2011 Coll. on specific health services, according to which the person collected blood for blood production for the production of blood derivatives and for human use according to other legal regulations and for its collection does not have the right to financial or other compensation, except for purposefully, economically and demonstrably spent expenses related to the collection of his blood, which this person requests, in total up to a maximum of 5% of the minimum wage.

Compensation policy of a donation centre in Austria

OVERVIEW PERSONAL TIME COMPENSATION

Your personal time compensation

For each donation in the Plasma Donation Center you will receive a 25 € compensation for your time spent. You can donate plasma up to 50 times per year.

Overview

The following compensations are provided for your time and loyalty.

DONATION 1-5	DONATION 6-10	DONATION 11-20	DONATION 21-30	DONATION 31-40	DONATION 41-50
25 EURO	25 EURO	25 EURO	25 EURO	25 EURO	25 EURO
25 EURO	25 EURO	25 EURO	25 EURO	25 EURO	25 EURO
25 EURO	25 EURO	25 EURO	25 EURO	25 EURO	25 EURO
25 EURO	25 EURO	25 EURO	25 EURO	25 EURO	25 EURO
25+15 EURO	25+15 EURO	25 EURO	25 EURO	25 EURO	25 EURO
Valid in the reference year:					
		25 EURO	25 EURO	25 EURO	25 EURO
		25 EURO	25 EURO	25 EURO	25 EURO
		25 EURO	25 EURO	25 EURO	25 EURO
		25 EURO	25 EURO	25 EURO	25 EURO
		25+15 EURO	25+15 EURO	25+15 EURO	25+40 EURO

DONATION NUMBER

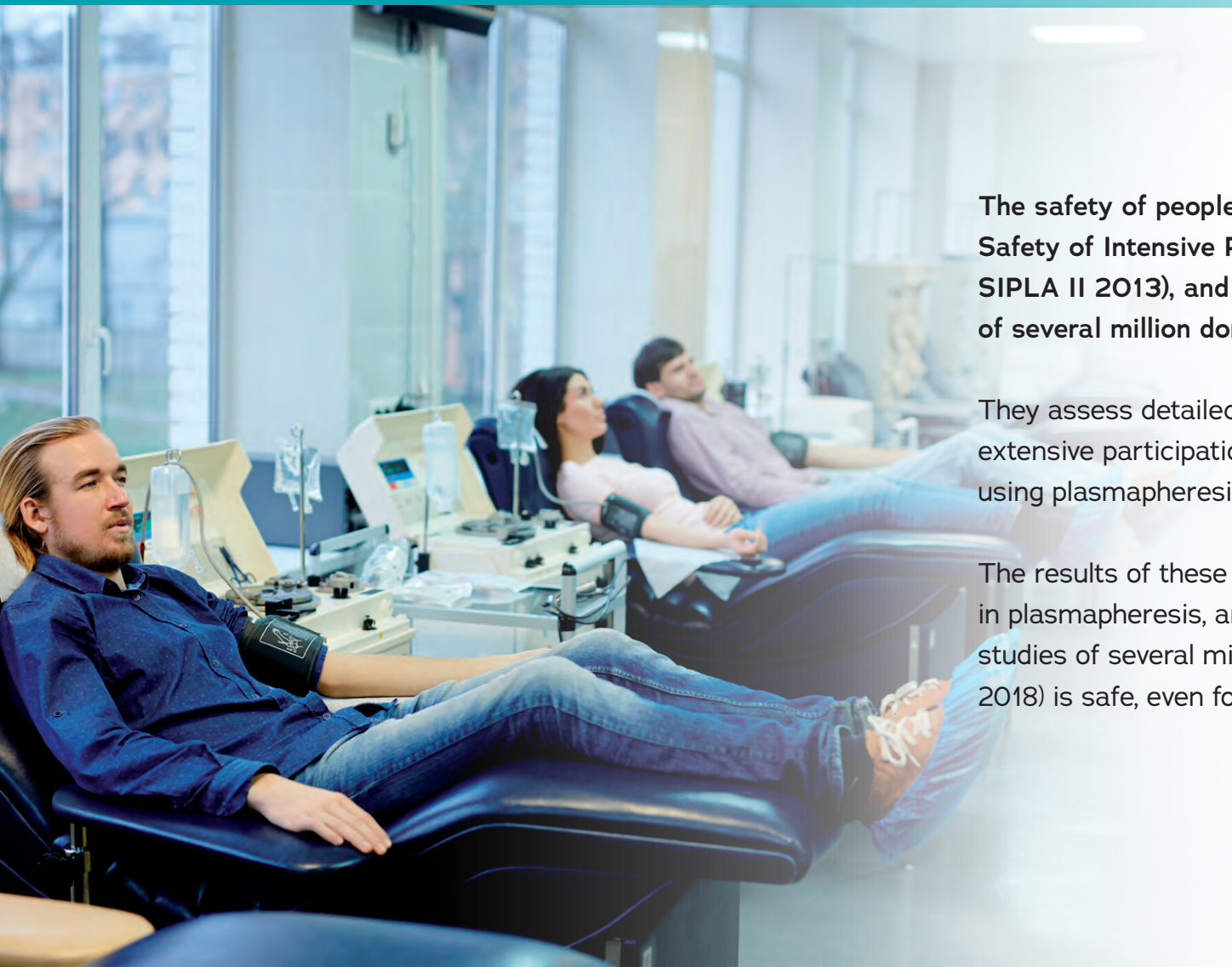
EXPENSE ALLOWANCE

BONUS

Compensation policy of a donation centre in Germany.

Donations made are voluntarily and generally free of charge. But as a permanent donor, you will receive a lump-sum allowance for the time you have spent in our blood donation centre.

9. Health & safety for donors



The safety of people donating plasma is tracked by the **Safety of Intensive Plasmapheresis studies (SIPLA I 2003; SIPLA II 2013)**, and further **European donor safety studies of several million donor experiences (PPTA 2016; 2018)**.

They assess detailed clinical data on the effect that extensive participation in the plasma donation process using plasmapheresis has on frequent plasma donors.

The results of these studies conclude that participating in plasmapheresis, and further European donor safety studies of several million donor experiences (PPTA 2016; 2018) is safe, even for first-time and inexperienced donors.

Donor Health & Safety

A range of European plasma donor studies have tracked the safety of intensive plasmapheresis, and analysed risk factors such as the intensity of donation, plasma volume per donation, frequency and the maximum plasma volume that one person can donate per year. The overall results show low risk and adverse events figures for the European donor population.

This body of evidence concludes²⁵:

- No significant adverse effects were registered on donor health by long-term intensified plasmapheresis if Hemoglobin, Total Protein and Immunoglobulin levels are monitored regularly.
- Donors and non-donors have equivalent humoral immune responses.
- Risk of adverse events decreases with the number of donations.
- Cardiovascular risk for donors is unaffected by plasmapheresis, evidenced by biochemical cardiovascular risk markers.
- Plasma donors have less Dialysis-Associated Encephalopathy than Whole Blood donors and Blood Platelet donors.

SIPLA 2 study concludes that plasmapheresis is safe (based on max. 60 donations/year & volume depending on body weight).

Cross-industry assessment of donor adverse events

A further study by PPTA analysed adverse events over millions of plasma donations tracked across plasma protein therapy producers. It found that the majority of donor adverse events observed were mild and the need for medical intervention was rare²⁶.

In Germany, guidance on donation frequency is set by the science-based data provided by the German Chamber of physicians.^{27, 28}

2016 Data Collection Study Highlights	
Data collection period	3 months in 2016
Total plasma donations	7.6 million (79% of industry)
Dialysis-Associated Encephalopathy (DAE) recorded	15,300
Overall DAE rate	2.09 per 1000 donations
Top 2 DAE Categories 75% of all Adverse Events (AE)	Hypotensive/vasovagal pre faint with no loss of consciousness (57% of all AEs). Local injury (hematoma/bruise) related to phlebotomy (18% of all AEs).
Most rare DAE categories	Severe hypotensive events (0.06 per 1000 donations) Hypotensive events with prolonged loss of consciousness (0.01 per 1000 donations) Hypotensive injury (0.007 per 1000 donations)
2018 Data Collection Study highlights (publication in preparation)	
Data collection period	4 months in 2018
Total plasma donations	12.5 million donations
Overall DAE rate	1.58 per 1000 donations
Top DAE Categories	Vasovagal
Rare occurrences	Medical intervention Donors needing transportation to the hospital within 24 hours, including donors who has AEs after leaving the donation centre (0.04 per 1000 donations).

Product safety in the plasma process

Plasma donation is a safe procedure. The donor screening and plasma protein therapy manufacturing processes ensure safety of final products. Over the past two decades no transmissions of blood-borne infections have been reported in association with the use of plasma protein therapies.

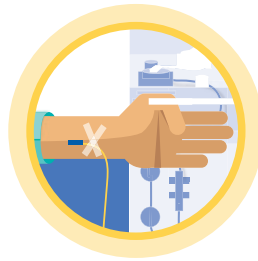
Plasma donors' health is protected by European regulations that govern the operation of plasma donation centres – including quality standards, the frequency and volume of donations for each donor, infrastructure and personnel requirements.

Plasma purity and safety is ensured by three processes in the pathway from plasma donation to manufacturing of plasma protein therapies:

- Donor screening and exclusion of high-risk donors
- Testing for virus pathogens
- Elimination of contaminants potential pathogens from the manufacturing process.

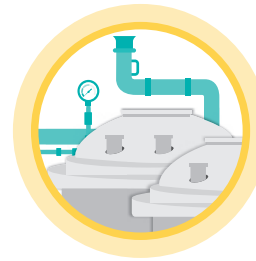
Plasma safety & purification process in medicines production

1. Donation



Only people passing rigorous safety screening are accepted as donors in plasma centres.

2. Pooling



Screening for a wide range of pathogens and viruses, including:

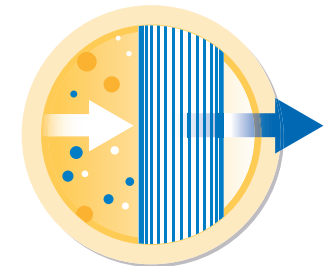
- Human immunodeficiency virus (HIV)
- Hepatitis B virus (HBV)
- Hepatitis C virus (HCV)
- Hepatitis A virus (HAV)
- Parvovirus B19

Further testing of manufacturing pool using Nucleic Acid Testing ensures that only plasma safe for medicines production moves into fractionation, where proteins are separated from the plasma.

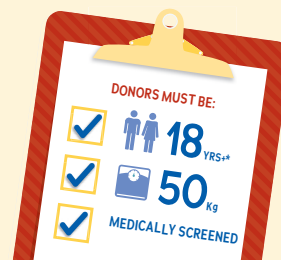
3. Purifying & Testing



4. Fractionation



The fractionation process includes further steps of contaminant removal and inactivation.



The PPTA independent Qualified Donor programme requires all prospective donors giving for use by its partners to have two satisfactory health screenings and negative test results within six months, before being authorized to give plasma.

Without meeting this requirement their plasma will not be used to manufacture plasma-derived medicines. This policy is important, firstly to protect donors' health and wellbeing, and to help ensure the quality and safety of the therapies that patients need to treat life-threatening diseases.

10. Risk factors: new treatment indications & external influences affecting Europe's stable access to plasma

Over the past three decades, European patients have benefited from stable access to plasma-derived medicines manufactured in Europe, delivered through national health systems, and based on a significant portion of plasma imported from US donors.

Today, the need for more plasma to produce medicines is growing. Improved and early diagnosis is helping more patients access treatment and medical research provides evidence for new indications for plasma-derived medicines.

At the same time, global emergencies such as the COVID-19 pandemic and geopolitical shifts driven by evolving national health priorities trade issues that may restrict the exchange of blood components and plasma protein therapies, may upend the current global balance for plasma exports and imports. What are the risk factors for Europe's public health policies?

External issues & risks – plasma in the geopolitical landscape

Ensuring stable plasma donations for this critical resource

Plasma and its derived medicines are a critical health resource that patients in every country need to manage and a wide range of critical health conditions.

Plasma is partly recovered from blood given to the national blood bank system, by donors giving plasma directly and partly imported from donors in other countries. In this light, emerging medical treatment trends and shifting politics that can affect the global health landscape risk disrupting access to the donated plasma – especially for plasma that is imported.

The sudden emergence of COVID-19 is an important lesson for plasma donation planning and risk management policies. While the donation situation in Europe has remained predictable over the years, the pandemic shows the reality of how the donation landscape can change rapidly and without warning. Overnight, the lockdown across Europe and globally in 2020 has severely reduced the number of donors and donations. The result was fewer donations of blood and plasma in most European countries.

Factors influencing increased need for plasma and derived medicines

The need for plasma to produce plasma-derived medicines has been growing steadily in recent years, driven by several factors:

- The increased precision of medical diagnostics means that more people are identified with conditions that these medicines can treat.
- More people are being diagnosed early and those under treatment are living longer.
- More clinical evidence is emerging to show the benefits of plasma-derived medicines to treat patients with a variety of disorders.
- Increased awareness helps lead early identification of rare diseases in many patients that can benefit from plasma-derived medicines.
- Progress of medical research²⁹ that identifies new areas where these medicines will bring life-changing and saving treatments, for example:
 - Immunoglobulins to boost immunity and prevent infections in patients with secondary antibody deficiencies caused by chemotherapy or immunosuppressive therapy.
 - Immunoglobulins in patients in pre- and post-allogeneic haematopoietic stem cell transplant.
 - Plasma to produce hyperimmune treatments that are highly effective against hepatitis A, measles, chickenpox and rubella. Plasma-derived medicines also show potential to control other types of viral infections; and for ‘passive immunity’ treatments, where plasma-based antibodies are given directly to patients.
 - Albumin to treat patients with decompensated cirrhosis.

National security – plasma in the geopolitical landscape

Growing interest in exploring the use of plasma and convalescent plasma for new treatments could open new treatment globally for plasma and its derived medicines – beyond the medicines specified today by countries' health services.

This new interest in the potential wider uses of plasma-derived medicines is evolving the thinking on how much plasma a country needs and where it will come from. These factors and the debate in public health systems on plasma's effectiveness for treating COVID-19 has placed this material as critical resource on countries' political and medical agendas. Some examples:

US national security plan. The 2012 US Presidential Order on National Defense Resources Preparedness calls for national health resources to be prioritized over the supply of foreign needs and contracts in the event of a national emergency. The health resources specified include drugs, biological products, medical devices, health supplies, services and diagnostic equipment. In a pandemic, plasma would be covered, raising the risk that exports could be curtailed.³⁰

COVID-19

The efficacy of plasma and its derived medicines as a treatment for COVID-19 have not been conclusive. To date it has shown to be effective only in the very early stages of the disease. Responding to the COVID-19 public health urgency in the pandemic's early days, some countries granted Emergency Authorization for plasma use. This has raised interest in the potential of convalescent plasma to treat the virus.

- This emerging situation, coupled with the use of plasma in treating Ebola, has heightened the perception that plasma can be considered to help manage future outbreaks – creating more interest among countries in securing a national plasma supply. This thinking may affect the global landscape for plasma donation in the medium term, and countries may include strategies to secure more plasma donations in their future pandemic preparedness plans.

- **US Food & Drug Administration – temporary authorization for plasma transfusions in COVID patients.** In mid-2020, the FDA authorized the emergency use of plasma donated by patients previously affected by COVID-19, for transfusions to treat affected patients.³¹ This was updated in March 2021 in a further Emergency Use Authorization by the FDA.³² It allows that COVID-19 convalescent plasma can be obtained from licensed blood establishments from donors in the US or its territories.

European Union policies/regulations on plasma self-sufficiency

The EU Blood Directive and related policies EU refer to an 'open strategic autonomy on starting materials for the manufacturing of medicines and to reduce the dependency from third countries' (see EU pharma and trade strategy).

ANNEX

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