Plasma Protein Therapies: Uniquely Saving Lives

Treating Rare Diseases

Plasma is the straw-colored liquid portion of blood. It contains hundreds of proteins, such as antibodies to fight diseases and clotting factors to control bleeding. If a person has insufficient levels of any one plasma protein, his or her body cannot carry out certain vital functions, causing a variety of chronic and life-threatening medical conditions.

Plasma protein therapies are unique biologic medicines that treat people with plasma protein deficiencies and dysfunctions. These disorders occur in a very small patient population and belong to a group of rare diseases. In Europe, a disease is considered rare if it affects 1 individual in 2,000.[1]

Your blood is:

- 55% PLASMA
- 44% RED BLOOD CELLS
- 1% WHITE BLOOD CELLS & PLATELETS

Your plasma is:

- 92% WATER
- 7% PROTEINS
- 1% OTHER SOLUTIONS

Examples of proteins in your plasma:

- IMMUNOGLOBULINS (ANTIBODIES)
- CLOTTING FACTORS
- C1 ESTERASE INHIBITOR
- ALPHA-1 PROTEINASE INHIBITOR

European patients in need of Plasma Protein Therapies (estimates)*

CAUSES & SYMPTOMS

PRIMARY IMMUNODEFICIENCY DISEASES (PID)

- Caused by missing or malfunctioning immunoglobulins (antibodies)
- Antibodies control the immune system and prevent illness
- Patients are chronically ill from severe, persistent, recurrent infections

375,000[2]

CHRONIC INFLAMMATORY DEMYELINATING POLYNEUROPATHY (CIDP)

- Cause not certain; immune system attacks nerve coating
- Messages from the brain aren't delivered to the body if nerve coating is damaged
- Patients experience progressive weakness, loss of limb function, and disability

33,750[3]

HAEMOPHILIA

- Caused by missing or malfunctioning clotting factor protein
- Clotting factors control bleeding
- Patients cannot regulate bleeding (joint damage is common)
- Can be fatal if bleeding occurs in brain or vital organs

150,000[4]

HEREDITARY ANGIO-OEDEMA

- Caused by missing or malfunctioning C1 esterase inhibitor protein (C1-INH)
- C1-INH helps control inflammation
- Patients have oedema (severe swelling)
- Can be fatal if airway obstructed

15,000[5]

ALPHA-1 ANTITRYPSIN DEFICIENCY

- Caused by missing or malfunctioning Alpha-1 Proteinase Inhibitor
- Alpha-1 Proteinase Inhibitor protects the lungs
- Patients have chronic emphysema and liver damage

75,000[6]

*Based on European population of 750,000,000.

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Made From Plasma

Donated Plasma Is A Finite Starting Material

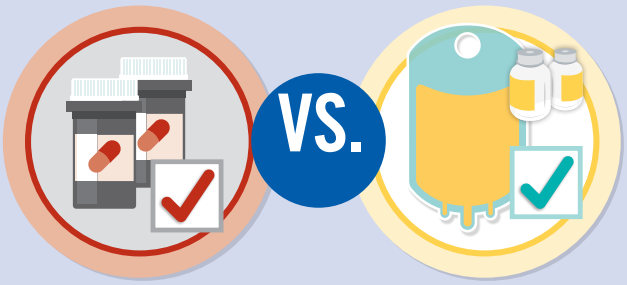
The starting material for plasma protein therapies is not an infinite resource. Rather than using synthetic or chemical ingredients, plasma protein therapies are made using human plasma. Plasma cannot be made synthetically in a laboratory. Plasma and its lifesaving proteins can only be obtained from donors who so generously give their time to donate.

PHARMACEUTICALS
Production begins with synthetic or chemical ingredients.

PLASMA PROTEINS
Production begins with a biological starting material (human plasma).

Authorization

EMA certifies establishments which collect plasma for manufacturing through the Plasma Master File (PMF) certifications, and thus qualifies its collection processes as to ensure they are carried out in line with the European regulations. In addition, each of these establishments is under separate supervision of the local and national regulatory authorities. In the European Union, all plasma-derived medicines are either centrally authorized by the European Medicines Agency (EMA), or by Member States' National Regulatory Authorities before they can be marketed.

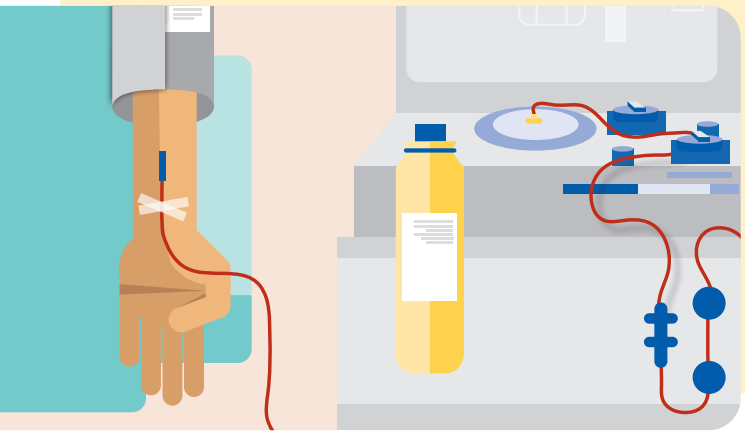


The authorization procedure for plasma proteins is different and more complex in comparison to the traditional chemical compounds.

Plasma Collection

Plasma is collected from healthy, mostly compensated donors through a process called plasmapheresis. Plasmapheresis removes a donor's plasma and returns the remaining cell components.

Plasma is collected at more than 100 plasma donation centers in the European Union. After collection, the plasma donation is frozen and shipped to a state-of-the-art facility for manufacture into lifesaving plasma protein therapies.



ESTIMATED DONATIONS NEEDED FOR ONE PATIENT FOR ONE YEAR:

130: PRIMARY IMMUNODEFICIENCY DISEASES

900: ALPHA-1 ANTITRYPSIN DEFICIENCY

1200: HAEMOPHILIA

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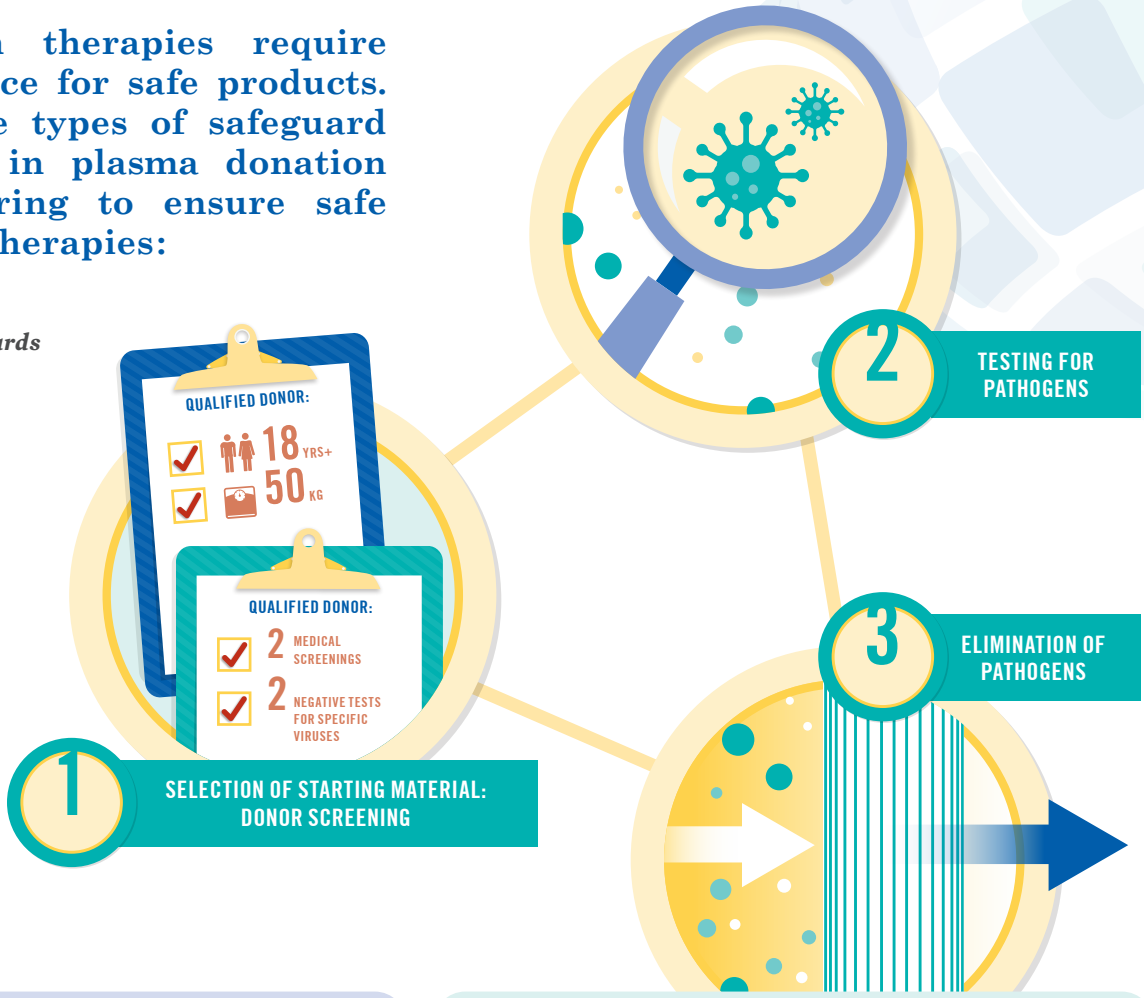
Constant Vigilance for Safe Products

Plasma protein therapies require constant vigilance for safe products. There are three types of safeguard measures used in plasma donation and manufacturing to ensure safe plasma protein therapies:

Voluntary industry standards often exceed regulatory requirements.

IQPP
INTERNATIONAL QUALITY PLASMA PROGRAM

QSEAL
QUALITY STANDARDS OF EXCELLENCE, ASSURANCE & LEADERSHIP



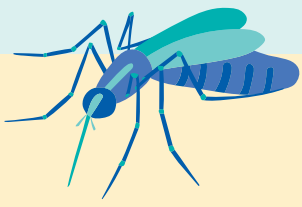
Current manufacturing protocols are extremely effective against pathogens.

The industry has a record of safety from pathogens for more than 20 years.[7]

Evolving Protocols

Unlike traditional pharmaceuticals or other biologics, ***plasma protein therapies' safety protocols are constantly evolving due to new and emerging pathogens.***

Companies must continuously perform tests to demonstrate that their viral inactivation and removal steps work on new pathogens. Most recently, companies invested significant time and resources into researching the Zika virus to ensure it does not threaten the safety of plasma protein therapies.[8]

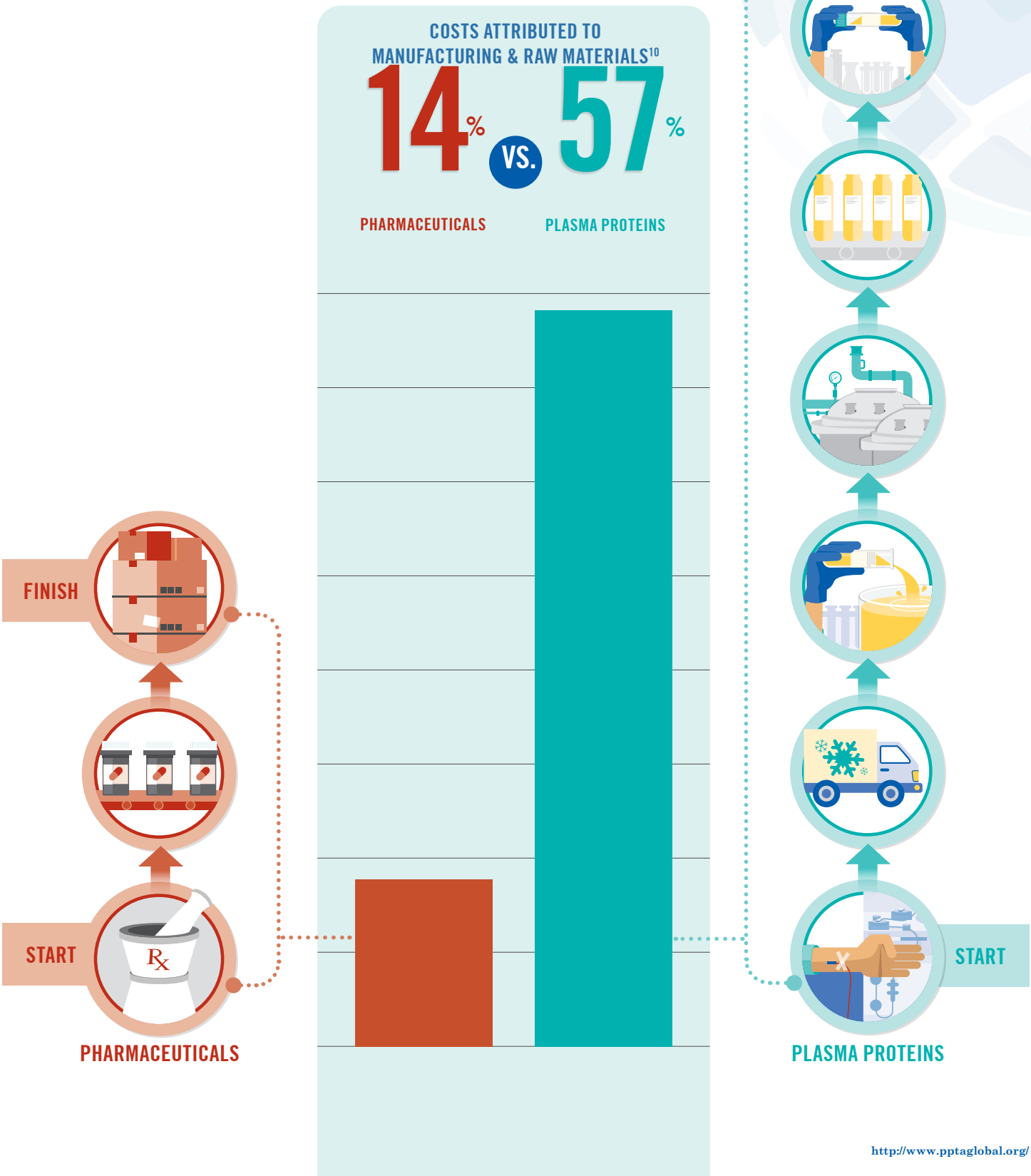


Plasma Protein Therapies: Uniquely Saving Lives

Uniqueness[9]

Plasma Protein Therapies are Highly Complex to Manufacture

Plasma protein therapies take **7-12 MONTHS** to manufacture. Companies must adhere to rigorous regulatory requirements to ensure manufacturing consistency and pathogen safety.



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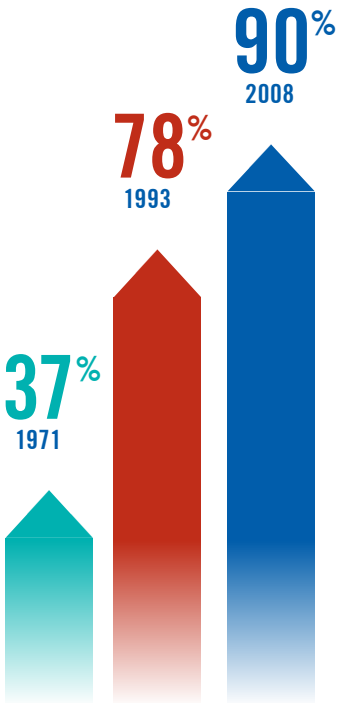
Value to Patients

As different policies to slow health spending are debated, it is critical to maintain access to lifesaving treatments for rare disease patients. A one-size-fits-all policy does not work for plasma protein therapies as these biologics are not interchangeable.

Plasma protein therapies increase life expectancy, improve quality of life, and reduce life-threatening complications for individuals with plasma protein deficiencies or abnormalities.

10-year survival rate of patients with COMMON VARIABLE IMMUNE DEFICIENCY, by year[11]



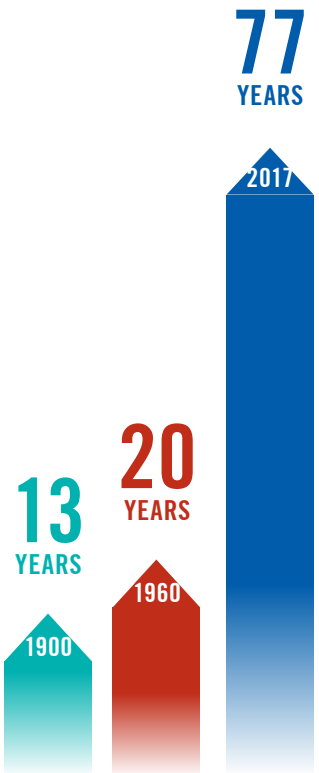
«Without treatment, I think my life would be quite different. [...] I know today that I am treated for nine years and my lungs are stabilized, that means I can do some sports, I can do my daily work as I would like to. I have a high quality of life because I have a lot of mobility, I can go wherever I want, I don't need a wheelchair, I don't need oxygen and I know also that tomorrow I will have the same quality of life as today.»

Frank, individual with Alpha-1 Antitrypsin Deficiency

«I was sick a lot and missed out on plenty of things kids my age were doing at that time. During my first year in college my condition worsened pretty fast, I couldn't keep up with others, and I was often on antibiotics. I received a diagnosis (CVID) in 2008 and my life changed completely once I began receiving immunoglobulin subcutaneously. I remember waking up in the morning and feeling full of energy like I honestly had never felt before. I am truly grateful for receiving a real chance at life.»

Janika, individual with Common Variable Immune Deficiency (PID disorder)

Life expectancy of a patient born with HAEMOPHILIA, by year[12]



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Non-Interchangeability

One-size-fits-all policies are unsuitable for plasma protein therapies and endanger patient health. Each therapy is non-interchangeable due to the pharmacologic and manufacturing differences that exist across different brands and patients' unique response to the treatments.

COUNCIL OF EUROPE
CONSEIL DE L'EUROPE

"[...] Take into account that human normal immunoglobulin therapeutic products differ from one another in terms of production processes, which might have an impact on specifications and clinical performance."[13]

IRIS

"Immunoglobulins are not interchangeable with each other, they are not generic medicines, prescribers must have long-lasting and readily available preparations."[14]

Health Canada

"Intravenous Immunoglobulin (IVIG) preparations are not considered identical, and no consideration can be given to approve a specific IVIG product, based on the proven safety and efficacy in established indications for other marketed IVIG products."[15]

IPOPI
INTERNATIONAL PATIENT ORGANISATION FOR PRIMARY IMMUNODEFICIENCIES

"It is important to realize that there is no single immunoglobulin (Ig) product or method of administration that is suitable for all PID patients. [...] All countries and immunodeficiency centers should have access to a wide spectrum of Ig products, to provide optimal treatment for all immunodeficient patients."[16]

UK Department of Health

"Although the active ingredient in IVIg - purified immunoglobulin - is the same from brand to brand, there are considerable differences in the manufacturing processes used. This results in individual products that cannot be used interchangeably."[17]

NATIONAL HEMOPHILIA FOUNDATION
for all bleeding and clotting disorders

"It is critical that the bleeding disorder community has access to a diverse range of therapies and that prescriptions for specific clotting factor concentrates are respected and reimbursed."[18]

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5. David M. Lang et al. "International consensus on hereditary and acquired angioedema", Annals of Allergy, Asthma & Immunology, Volume 109, Issue 6, December 2012, Pages 395-402
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10. Marketing Research Bureau 2011
11. Chapel H, Lucas M, Lee M, et al. Common variable immunodeficiency disorders: division into distinct clinical phenotypes. Blood. 2008; 112(2):277–286.
12. Aledort, L. The evolution of comprehensive haemophilia care in the United States: perspectives from the frontline. Haemophilia. 2016; 22(2) 676–683.
13. Council of Europe, Resolution CM/Res(2015)2 on principles concerning human normal immunoglobulin therapies for immunodeficiency and other diseases (Adopted by the Committee of Ministers on 15 April 2015 at the 1225th meeting of the Ministers' Deputies)
14. Immuno-déficience primitive, Recherche, Information, Soutien (I.R.I.S.) Position Statement Summary http://www.associationiris.org/archives-des-articles?&w[actualites-archives_l][startnum]=-10
15. Health Canada Effective Date: 2004/08/04 http://www.hc-sc.gc.ca/dhp-mps/alt_formats/hpfb-dgpsa/pdf/brgtherap/ivig-igiv-eng.pdf
16. Frontiers in IMMUNOLOGY, Primary Immune Deficiencies – Principles of care; Hypothesis and Theory Article, published: 15 December 2014, doi: 10.3389/fimmu.2014.00627
17. Clinical Guidelines for Immunoglobulin Use; the UK Department of Health, 2008, p. 15
18. National Hemophilia Foundation, Medical and Scientific Advisory Council Recommendation #159

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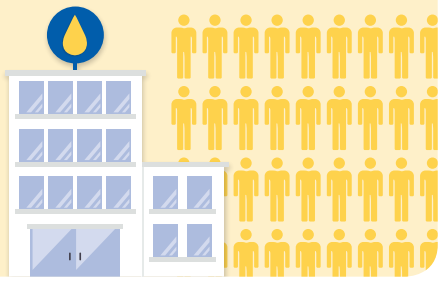
    https://www.hemophilia.org/sites/default/files/document/files/masac159.pdf

186 PLASMA DONATION CENTERS BUT MORE EUROPEAN PLASMA IS NEEDED.

Employment

Each plasma donation center employs between 15 - 30 people.



Collection Center Impact on Local Economies

Plasma donation centers support local economies through center staff jobs, facilities, equipment, taxes, and donor compensation.

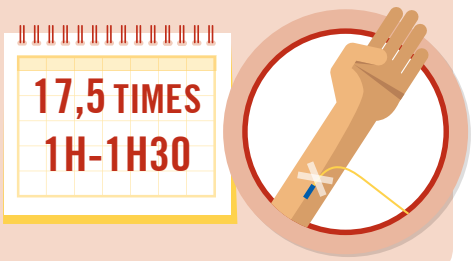
EPA Collection

More than 2,5 million liters of plasma are donated annually in Europe.

2,5 MILLION

Repeat Engagement

On average, a donor donates 17,5 times per year, for an hour to an hour and a half.



PPTA
Plasma Protein Therapeutics Association

European Plasma Alliance (EPA)

The EPA is an alliance of 10 European private sector plasma collectors:

- Biopharma-Plasma Blood Service Center
- Europlasma
- Haema (Grifols)
- KEDPLASMA
- Octapharma
- Plasma Place
- Plasmavita
- Prothya Biosolutions
- Takeda
- Unicaplasma

Global Members

Biotest

bpl
Bio Products Laboratory

GRIFOLS

KEDRION
BIOPHARMA

Takeda

January 2023

http://www.pptaglobal.org/