

# Plasma

## The Patients Perspective



Brian O'Mahony,

PLUS (Plasma Users)

FIODS Conference, San Marino

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# PLUS (Plasma Users)



Guillain-Barré Syndrome • Chronic Inflammatory Demyelinating Polyneuropathy



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**REPORT**

## The Dublin Consensus Statement 2011 on vital issues relating to the collection and provision of blood components and plasma-derived medicinal products

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Following a conference in Dublin in 2010, a consensus statement was published in this journal [1]. In January 2011, a follow-up conference was convened in Dublin under the auspices of the plasma users coalition (PLUS) to further consider the statement produced in Dublin in 2010. The goal was to negotiate a revised set of principles which could be potentially accepted by most stakeholders including global patient, donor, manufacturing and provider organisations. PLUS was eager to continue the constructive dialogue that commenced between key stakeholders in 2010.

PLUS represents the concerted views of seven patient organisations, whose members are dependent on products manufactured from plasma. The goal of PLUS in this work is to help encourage the production of a sufficient supply of safe and effective plasma-derived medicinal products (PDMPs) to meet the global needs of patients, by recognising that the collection systems for blood components and PDMPs are interrelated in a number of countries, thus ensuring coordinated collection of both blood and plasma and the manufacture of PDMPs from both the industry and not-for-profit sectors, and the status of national blood authorities, patient and donor organisations.

The meeting was attended by the following persons representing organisations as follows:

PLUS members: Brian O'Mahony (Chairman) - European Haemophilia Coalition (EHC) and Irish Haemophilia Society, David Watkins (POPL), Larry Warren, John Pezzot (POPL), Uwe Schlotterbeck (EHC), David Page (WHF).

Other participants: Mark Skinner (A-PLUS) and World Federation of Hemophilia (WFH), Chadwick Walker and Albert Fariaga - Plasma Protein Therapeutics Association, Bob Perry and Theo Fyvie - International Plasma Fractionation Association (IPFA), Roger Dodd - International Society of Blood Transfusion, Nilsa Mikellén - International Federation of Blood Donor Organisations (IFBDO), Drs MacPherson - America's Blood Centers, Alison Turner - National Blood Authority Australia, Patrick Robert-Markling - Research Bureau (Gen) and Prof KIDGM, Paul Stronger - SHF / Sangvis, Ulrike Follmer - European Blood Alliance (EBA).

A number of other organisations were invited to send representatives, including WHF, Thalassemia International Federation and the International Federation of Red Cross and Red Crescent Societies but were unable to attend because of other commitments.

The statement produced in 2010 had been fully endorsed by 22 patient organisations and was endorsed with qualification by a number of other key stakeholder organisations. The most significant qualification raised by organisations related to the previous clause 2.11 which was interpreted by some as providing endorsement for paid donations. Organisations that operate within a framework that only supports unpaid donors were therefore unwilling to fully endorse the 2010 statement. Not unexpectedly, this issue occupied a significant amount of time at the 2011 meeting. The final wording agreed recognises that different organisations will operate within different policy and regulatory frameworks, but acknowledges that both systems are needed at the current time. Encouragingly, there has emerged an improved understanding and dialogue between paid and non-paid system advocates of the need for both

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# Conditions treated with PDMP's

- Haemophilia – A and B
- Von Willebrands Disease
- Rare bleeding disorders
- Primary Immune Deficiencies (PID)
- Alpha 1 anti trypsin deficiency
- Guillain Barre Syndrome
- Idiopathic Thrombocytopenic Purpura
- Hereditary Angiodema

# WHO Essential Medicines List

- Plasma derived FVIII for Haemophilia
- Plasma derived PCC for FIX deficiency
  
- Normal Human Immunoglobulin ( IV and IM)
- Anti D Immunoglobulin
- Anti- tetanus immunoglobulin

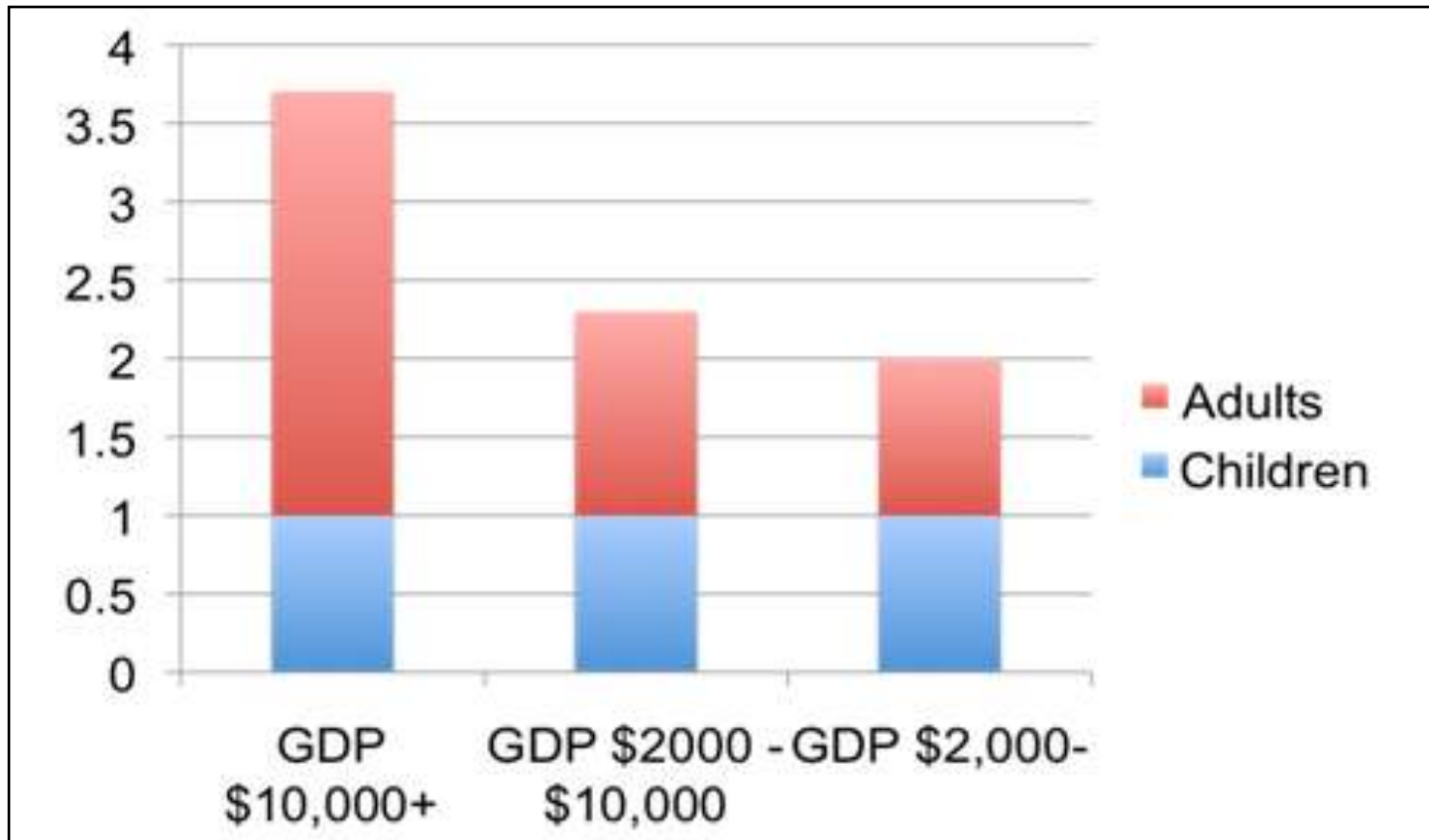
# Haemophilia

- Estimated 400,000 – 600,000 worldwide
- 153,251 diagnosed ( 2009)
- 62,158 with von Willebrands diagnosed
  - 70% untreated globally
  
- PID- estimated up to 1.4 million people
  - 80% untreated globally

# Haemophilia: Impact of lack of treatment

- Death – often in childhood
- Crippling arthropathy
- Risk of blood borne viruses from unsafe treatment
- Failure to complete education
- Lack of employment or family opportunities
- Requirement for orthopaedic surgery
- Dependant on society rather than contributing to society

# Ratio of adults to children / economy





# Impact of Poor treatment





# Impact of Treatment



# Impact of Good Treatment







# Impact of lack of treatment for PID's

- Death
- Constant life threatening or life impairing infections
- Long term damage
- Severe restrictions to activities and quality of life

# Impact of Lack of treatment for PID's



# Impact of Treatment for PID's





# Replacement Therapy Objective

*Sufficient quantity of Factor Concentrate should be available to each person with haemophilia or Immune Globulin to each person with PID to allow them to optimise their quality of life, achieve their potential with regard to education, employment and family and take a full and active role in society*

# Disparity in Haemophilia treatment around the world

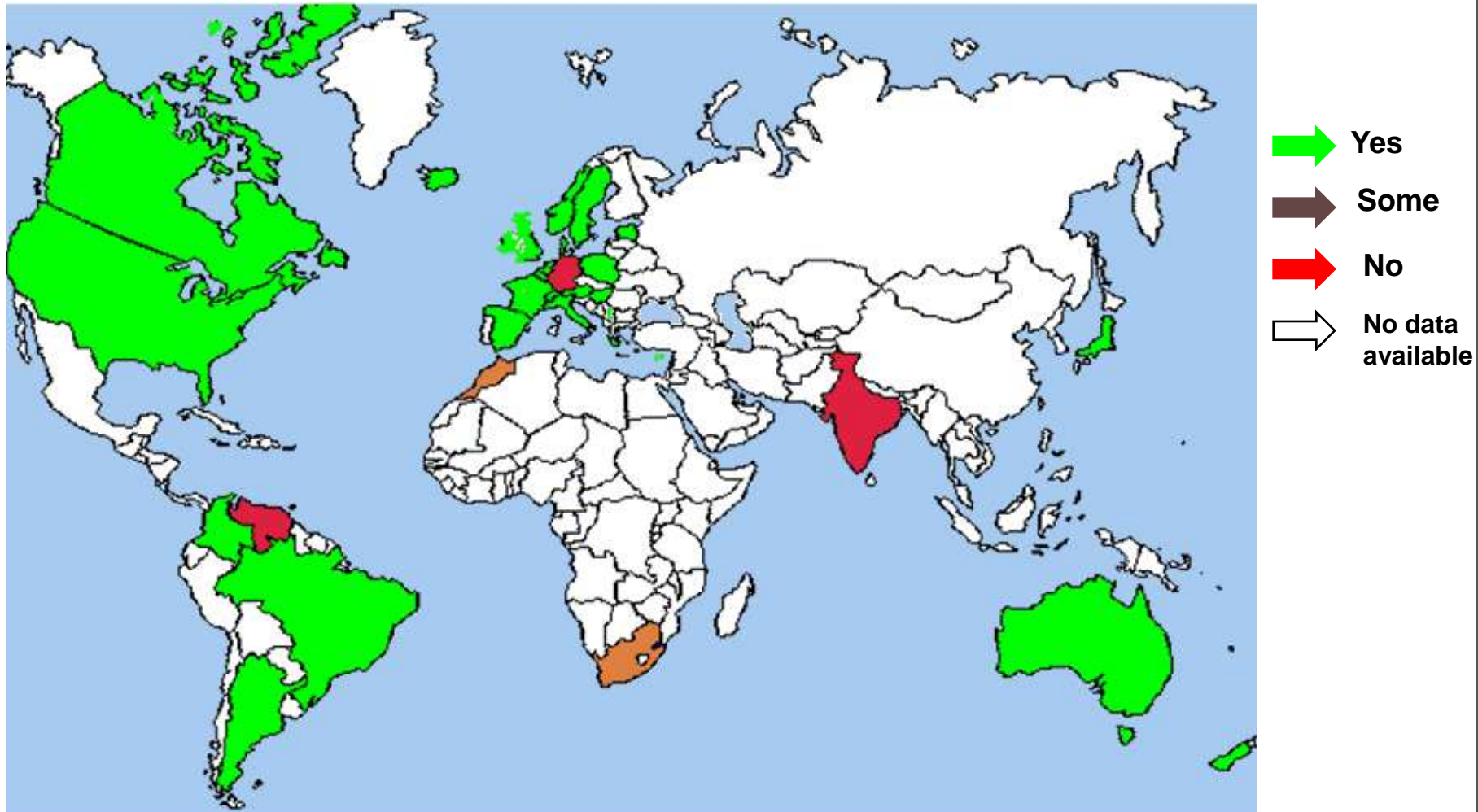
Economy	IUs per capita (average)	Increase to reach level of high income countries
High income economies	5.36	—
Upper middle income economies	1.42	x 3.7
Lower middle income economies	0.28	x 19
Low income economies	0.02	x 268

# Disparity in Haemophilia Treatment Globally

Country	Economy	IUs/capita	IUs per PWHA
<b>Sweden</b>	<b>High</b>	<b>6.9</b>	<b>85,000</b>
<b>Germany</b>	<b>High</b>	<b>6.7</b>	<b>138,000</b>
<b>Australia</b>	<b>High</b>	<b>4.6</b>	<b>68,000</b>
<b>Hungary</b>	<b>Upper middle</b>	<b>5.1</b>	<b>65,000</b>
<b>Russia</b>	<b>Upper middle</b>	<b>2.9</b>	<b>52,000</b>
<b>Turkey</b>	<b>Upper middle</b>	<b>1.0</b>	<b>24,000</b>
<b>Iran</b>	<b>Lower middle</b>	<b>1.3</b>	<b>22,000</b>
<b>Colombia</b>	<b>Lower middle</b>	<b>0.74</b>	<b>29,000</b>
<b>Peru</b>	<b>Lower middle</b>	<b>0.1</b>	<b>7,000</b>
<b>China</b>	<b>Lower middle</b>	<b>0.03</b>	<b>NA</b>
<b>India</b>	<b>Low</b>	<b>0.007</b>	<b>1600</b>
<b>Senegal</b>	<b>Low</b>	<b>0.002</b>	<b>400</b>

Source: A Study of Reported FVIII Use Around the World, J.S. Stonebraker et al, Haemophilia (2010), 16, 33-46

# IPOPI Survey: Provision of Care for Adult Patients With PID – Country Spilt



# Demand Trends 1984-2010

- Demand for Plasma derived FVIII has increased moderately – constrained by availability of recombinant FVIII
- Demand for Albumin has increased moderately
- Demand for IVIG has greatly increased –  
From 7 to 95 tons

**IVIG demand now the main driver for plasma collection**

# Projected Demand to 2020

- Plasma derived FVIII demand to increase from 3.2 to 4.3 Billion IU
- IVIG demand to increase from 95 to 216 tons
- **Current global supply of plasma for fractionation:  
32.7 million litres**

## **Plasma Source ( Mil/L)**

- North America 18,803 (57%)
- Europe 7,726 (24%)
- Asia/Oceania 5,320 ( 16%)
- Latin America 588 (2%)
- Middle East / Africa 291(1%)

**74%= Pheresis plasma**



# Future Plasma Demand

- If IVIG not approved for Alzheimers:  
Supply requirement will rise to 37.6 million litres by 2018
  - **additional 4.9 million litres**
  - **10.8 million donations**
- If IVIG is approved for Alzheimers: Supply requirement will rise to 47.8 million litres by 2018
  - **additional 15.1 million litres**
  - **33.5 million donations**

Source: MRB

# Possible Developments

- Increased need for IVIG for PID
- Possible use of IVIG for Alzheimers
- Requirement for up to 15 million additional litres of plasma per annum
- Source or recovered ?
  - Both required
  - supply has to be increased and optimised

# Conclusion

- **There is a need for...**
  - Increased global plasma collection and fractionation into PDMPs
  - Enhanced regulatory capacity in developing countries to make the best use of recovered plasma
  - Improved and optimised yields
  - Recognition that supply is a safety issue

# Conclusion

Requirement for increased plasma supply:

- From repeat well characterised paid plasmapheresis donors
- From repeat well characterised unpaid plasmapheresis donors
- From recovered plasma from voluntary blood donors
- From optimising utilisation and fractionation of plasma currently collected and underused or discarded if from well regulated system
- Safety paramount

# Dublin Consensus Statements

## REPORT

### The Dublin Consensus Statement on vital issues relating to the collection of blood and plasma and the manufacture of plasma products

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<sup>1</sup>Irish Haemophilia Society, Steering Group PLUS, Cathedral Court, Dublin, Ireland

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## Vox Sanguinis

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The requirement for plasma products manufactured from both source and recovered plasma for the treatment of many medical conditions is projected to increase substantially in the course of the next 5 years [1]. Patient organizations representing many thousands of patients with rare disorders who are dependant on products manufactured from plasma formed a coalition of plasma users- PLUS- in 2009. PLUS represents the concerted views of seven organisations, the International Patients Organisation for Primary Immunodeficiency (IPOP), the World Federation of Hemophilia (WFH), the European Haemophilia Consortium (EHC), Alfa Europe, Idiopathic Thrombocytopenic Purpura Support Organisation (IIP), Hereditary Angiodema International (HAIE) and Guillain Barre Syndrome Foundation International (GBS/CIDP).

Over the last thirty years, the manufacture from plasma of an increasing range of stable clinical products and the availability of plasmapheresis collection technology has led to the development of a commercial industry based on plasma-only donations from remunerated donors. In countries that do not permit a remunerated donor system, plasma collections are limited to those collected by blood establishments operating with non- remunerated donors. The growing global requirement for safe and effective plasma products [1] to meet the health needs of patients mean that plasma from both the commercial plasma and the blood sectors are essential to provide the range and

quantity of plasma products required. IPOP estimate that < 15% of persons with primary immune deficiency worldwide are diagnosed and treated [2]. In 2007, there was a total of 26.5 million litres of plasma available for fractionation including 8.6 million litres of recovered plasma and 17.9 million litres of source plasma [1]. It is estimated that the global requirement for plasma for fractionation by 2015 may be 41.7 million litres even in the absence of any new indications for IVIG [1]. Patients who are dependant on these life-saving therapies want to be reassured that they will have access to a sufficient supply of safe and effective therapy manufactured from the plasma of carefully selected and tested donors in the future.

National policies in most cases only permit a non- remunerated system of blood and plasma collection. This means that commercial plasma collections are limited to a few countries which allow both remunerated and non- remunerated donations including the United States of America, Germany, Czech Republic and Austria. Most countries utilize domestic non- remunerated blood collection to fully satisfy their requirements for labile blood components. However, the vast majority of these countries also import additional products from the commercial plasma sector to fully meet their health needs.

The plasma fractionation sector comprises both commercial and not for profit manufacturers, and these compete in both global and national markets. Where both commercial and not for profit plasma collection or manufacturing systems coexist or compete at a national level, there can be tensions and disagreements between the sectors on issues such as the relative safety profile of remunerated and non- remunerated donors, as well as competition for donors.

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PLUS represents the concerted views of seven patient organisations, whose members are dependent on products manufactured from plasma. The goal of PLUS in this work is to help encourage the production of a sufficient supply of safe and effective plasma-derived medicinal products (PDMPs) to meet the global needs of patients. By recognising that the collection systems for blood components and PDMPs are interrelated in a number of countries, this meeting considered the collection of both blood and plasma and the manufacture of PDMPs from both the industry and not for profit sectors, and the views of national blood authorities, patient and donor organisations.

The meeting was attended by the following persons representing organisations as follows:

PLUS members: Brian O'Mahony (Convenor) -European Haemophilia Consortium (EHC) and Irish Haemophilia Society, David Watters-IPOP, Larry Warren, Johan Prevot-IPOP, Uwe Schlenkrich-EHC, David Page-WFH,

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# Dublin Consensus 2011- Patients

- Meeting the health needs of patients through a sufficient supply of safe and effective blood components and PDMPs is the principal goal of blood establishments and the plasma industry. An insufficient supply is a major safety risk to patients.
- Patients are entitled to expect that all stakeholders will support their need for access to safe and effective products.



# Dublin Consensus 2011- Donors

- Blood establishments and the plasma industry must respect the intrinsic dignity of all people involved in the blood and plasma donation process.
- Blood establishments and the plasma industry and society in general should highly value all those who donate blood or plasma for the benefit of patients, recognize that donors perform a good deed and treat donors with respect.

# Dublin Consensus 2011- Donors

- All people may offer blood or plasma to the community and their generosity is highly valued. However, blood establishments and the plasma industry have an obligation to only accept blood or plasma where the donor selection criteria are met.
- All donors must be provided with clear and accessible information prior to their donation, which should include information on:
  - The potential risks to them of donating blood or plasma,
  - The intended use of their donation,
  - Who might benefit from their donation,

# Dublin Consensus 2011- Donors

- All donations should be voluntary.
- All donors must give their free and informed consent prior to the donation.
- Donors should not be exploited by any individual or organization. Measures and initiatives taken to encourage blood and plasma donations should not overwhelm the capacity of the donor to make an informed decision about whether or not to donate.
- Blood establishments and the plasma industry owe a professional duty to act in the best interests of those that donate and receive blood and PDMPs.
- The health of the donor should not be compromised by their donation.

# Dublin Consensus 2012

## Recommendations

- Increase global plasma collection
- Enhance regulatory capability in developing countries
- Widen access to manufacturing technology
- Harmonise international regulation of blood/plasma collection
- Recognition that supply is a safety issue

# Dublin Consensus 2012

## Recommendations

- Promote National treatment protocols and indication prioritization mechanisms prepared in collaboration with national patient organizations
- Recognition that both private and public sectors are needed to meet global demand for plasma derived products
- Recognition that the use of the evidence base for the use of PDMPs in the treatment of rare disorders must be practicable and pragmatic

# Optimum treatment for 1 adult

## **Haemophilia A**

- 70kg man- 30IU/Kg/ 3times per week
- 327,000 IU
- 200 IU per litre of plasma
- 1,638 litres of plasma
- *3,640 donors*

## **Primary Immune Deficiency**

- 1 gram/KG/week – 70 gram/week
- 3,640 grams – 4g/litre plasma
- 910 litres plasma
- *2,020 donors*

# Conclusion

- Present and future demand for Plasma greatly exceeds demand for red cells
- Should dispense with arguments about which sector needed- clearly both are needed
  - Source and recovered plasma
  - Paid and unpaid plasma donors

**Growing appreciation of reality and partnership and mutual understanding between donor organisations and patient organisations**