INTERNATIONAL PLASMA FRACTIONATION ASSOCIATION

• Aligns its activities with the needs of all patients dependent on blood and plasma products and other donations of human origin.
• Aligned with wider Public Health considerations of healthcare resources.
• Not for Profit
• VNRBD and recovered plasma
• Nationally mandated/focused member organisations
• Evolved from traditions of Self Sufficiency
Self Sufficiency – What does it mean?

- A wicked invention to frustrate global markets and patient needs?
  Or

- A desirable and achievable goal reflecting the very best qualities of human morality?
  Or

- An important component of a global, regional and national strategy to safeguard the interests of all patients in a particular geographical community.

AND CAUTION

Advocacy for (self) sufficiency does not translate into uncompromising opposition to everything else!
The Canadian Model

Canadian Sufficiency in Plasma Products

How much product from Canadian Plasma?

self-sufficiency is no longer the goal for Canadian Blood Services

defining the appropriate level of IVIG sufficiency for Canada is based on mitigating the risk of disruption to the supply of IVIG

supply of raw material. Canadian plasma is a different source of raw material than US plasma, therefore the purchase of US plasma for fractionation to achieve IVIG sufficiency is not a valid risk to mitigate this risk, i.e. retain certain control over the supply chain with Canadian plasma

supply of fractionation capacity. seek to have two fractionators licensed for Canadian plasma

should be reasonable, practical and attainable within 5 years, and sustainable
4. TRENDS IN ISSUE OF IVIG - 2003/04 TO 2010/11

The total volume of IVIg issued under the National Blood Arrangements continued to increase during 2010/11 (Figure 1). A total of 2,950,371 grams were issued nationally in 2010/11 - an increase of 295,186 grams over 2009/10. Of this total, 14% was imported product.

However, the increase in growth nationally is lower than in previous years, suggesting the rate is slowing (Table 1 below).

Table 1

<table>
<thead>
<tr>
<th>Year</th>
<th>Growth from previous year</th>
<th>Average growth from 2003/04</th>
</tr>
</thead>
<tbody>
<tr>
<td>2003/04</td>
<td></td>
<td>4.7%</td>
</tr>
<tr>
<td>2004/05</td>
<td>16.2%</td>
<td>9.5%</td>
</tr>
<tr>
<td>2005/06</td>
<td>13.9%</td>
<td>10.3%</td>
</tr>
<tr>
<td>2006/07</td>
<td>13.5%</td>
<td>11.5%</td>
</tr>
<tr>
<td>2007/08</td>
<td>10.5%</td>
<td>12.0%</td>
</tr>
<tr>
<td>2008/09</td>
<td>11.6%</td>
<td>11.7%</td>
</tr>
<tr>
<td>2009/10</td>
<td>11.1%</td>
<td></td>
</tr>
<tr>
<td>2010/11</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Source: IDMS database of issues via Big Red

Average growth is the fixed rate of growth each year that would accumulate from 2003/04 to give the year's value. It is obtained by the formula $V_n = V_0(1+g)^n$; where $V_n$ = volume in year $n$.
## PLASMA COLLECTED IN 2008 (000’s liters)
(source: EU Commission + MRB – Marketing Research Bureau)

<table>
<thead>
<tr>
<th>Country</th>
<th>Non Remunerated</th>
<th>Remunerated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Austria</td>
<td>109</td>
<td>300</td>
</tr>
<tr>
<td>Belgium</td>
<td>163</td>
<td>Not allowed</td>
</tr>
<tr>
<td>Denmark</td>
<td>73</td>
<td>Not allowed</td>
</tr>
<tr>
<td>Finland</td>
<td>69</td>
<td>Not allowed</td>
</tr>
<tr>
<td>France</td>
<td>770</td>
<td>Not allowed</td>
</tr>
<tr>
<td>Germany</td>
<td>1079</td>
<td>1419</td>
</tr>
<tr>
<td>Greece</td>
<td>15</td>
<td>Not allowed</td>
</tr>
<tr>
<td>Italy</td>
<td>648</td>
<td>Not allowed</td>
</tr>
<tr>
<td>Ireland</td>
<td>Plasma collected is discarded</td>
<td>Not allowed</td>
</tr>
<tr>
<td>Luxemburg</td>
<td>8</td>
<td>Not allowed</td>
</tr>
<tr>
<td>Netherlands</td>
<td>294</td>
<td>Not allowed</td>
</tr>
<tr>
<td>Portugal</td>
<td>Plasma collected is discarded</td>
<td>Not allowed</td>
</tr>
<tr>
<td>Spain</td>
<td>321</td>
<td>Not allowed</td>
</tr>
<tr>
<td>Sweden</td>
<td>174</td>
<td>Not allowed</td>
</tr>
<tr>
<td>U.K.</td>
<td>Plasma collected is discarded</td>
<td>Not allowed</td>
</tr>
<tr>
<td><strong>Total 15 countries</strong></td>
<td><strong>3723</strong></td>
<td><strong>1719</strong></td>
</tr>
</tbody>
</table>

**Total:** 5,442
Plasma collection and self-sufficiency

Self-sufficiency for plasma derived products = self-sufficiency for Immunoglobulins

<table>
<thead>
<tr>
<th>IG Usage in 2008 (Kgs)</th>
<th>Plasma needed (000's l) for self-sufficiency with production yield</th>
<th>Plasma collected</th>
<th>Self-sufficiency ratio if yield = 4.0 g/l</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>4.0 g/l</td>
<td>4.2 g/l</td>
<td>Non remun.</td>
</tr>
<tr>
<td>Total 15 countries</td>
<td>21991</td>
<td>5498</td>
<td>5236</td>
</tr>
<tr>
<td>Total 13 excl. UK &amp; Ireland</td>
<td>18826</td>
<td>4706</td>
<td>4482</td>
</tr>
</tbody>
</table>

With a production yield of 4.0 g/l, the 15 countries are self-sufficient with the plasma they collect. When taking into consideration the UK & Ireland decision not to use European plasma, the other 13 countries can be more than self-sufficient and the non-remunerated plasma covers ≈ 80% of their needs.
Where are we now?

• Plasma derivatives are as safe as they can be
• Plasma from paid and unpaid donors is suitable for manufacture (if collected in well regulated environment)
• Full range of products available to EU patients – if affordable
• No shortages
• Free and open competitive environment exists for product supply to EU countries
The Dublin Consensus Statement 2011 on vital issues relating to the collection and provision of blood components and plasma-derived medicinal products

B. O’Mahony1 & A. Turner2
1Chief Executive, Irish Haemophilia Society, Steering Group PLUS, Dublin 8, Ireland
2Chief Executive, National Blood Authority, Canberra, Australia

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 organisations 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 including the European Haemophilia Consortium (EHC), the American Rare Blood Factor Patients Organisation (FRDO), Alfa Europe, Idiopathic Thrombocytopenic Purpura Support Group (ITP), Hereditary Angiodema International (GBS), the European Haemophilia Society, Steering Group PLUS, Cathedral Court, New Street South, Dublin 8, Ireland, and the International Federation of Red Cross and Red Crescent Societies. Since its formation, PLUS has worked towards the establishment of a consensus on the collection of blood and plasma and the manufacture of plasma products [1]. 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, donors, manufacturing and provider organisations. PLUS was eager to continue the constructive dialogue that has emerged an improved understanding and dialogue between systems coexist or compete at a national level, there can be occasions on which these systems have to operate in parallel [1]. The outcome of this process was the Dublin Consensus Statement on vital issues relating to the collection of blood and plasma and the manufacture of plasma products published online 2 August 2011.

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Where is there consensus?? - PLUS
Where is there consensus??

Recognition of:-

• All contributions to plasma/product supply.
• The central importance of patient needs and evidence base for planning/strategies
• Interests of all patients dependent on donations of human origin.
• Contributions to global supply through national/regional strategies.
• Optimal use protocols.
• Patient involvement.
• Strengthening regulatory expertise.
• Etc.
So.......What is the Problem?

• Increasing demand for pdmp from both developed and developing countries – both existing and new indications.
• Wastage of plasma.
• Strategies to safeguard EU supplies.
• Diminishing health care budgets.
Unequal Global Access

World Population by Region - 2010

- Asia & Pacific: 58.1%
- Europe: 28.6%
- South America: 8.7%
- Middle East & Africa: 17.4%
- North America: 5.0%

THE IVIG/SCIG MARKET IN VOLUME BY REGION - 2008

Total Market 81.9 Metric Tons

- Europe: 28.6%
- Asia & Pacific Oceania: 13.8%
- Middle-East Africa: 3.2%
- South America: 4.4%
- North America: 49.9%
IgG Consumption in Europe per capita - 2009

Data Sources:
- Europe & USA: PPTA Data - 2009
By 2050 healthcare spending will have risen to 40% GDP!!

Source: OECD
Accessed 2012-09-10 18:20
Figure 2. Average annual growth in health spending across OECD countries in real terms, 2000-2010

Note:
Growth rates for 2009/10 are not available for Australia, Japan, Luxembourg, Israel, Spain and Turkey.
Growth rates for Chile calculated using the Consumer Price Index (CPI).

Source: OECD Health Data 2012
Plasma collection vs healthcare resources vs patient access
## Immunoglobulin Use in European Countries 2008

Does high plasma collection guarantee patient access?

<table>
<thead>
<tr>
<th>Country</th>
<th>Use g/1000 population</th>
<th>Country</th>
<th>Use g/1000 population</th>
</tr>
</thead>
<tbody>
<tr>
<td>Belgium</td>
<td>97.1</td>
<td>Norway</td>
<td>36.8</td>
</tr>
<tr>
<td>Sweden</td>
<td>93.8</td>
<td>AVERAGE</td>
<td>36.5</td>
</tr>
<tr>
<td>Ireland</td>
<td>79.6</td>
<td>Germany</td>
<td>36.4 (290%)</td>
</tr>
<tr>
<td>France</td>
<td>79.3</td>
<td>Czech Republic</td>
<td>23.2 (477%)</td>
</tr>
<tr>
<td>Austria</td>
<td>78.5</td>
<td>Slovakia</td>
<td>19.5</td>
</tr>
<tr>
<td>Denmark</td>
<td>72.8</td>
<td>Croatia</td>
<td>13.7</td>
</tr>
<tr>
<td>Finland</td>
<td>70.4</td>
<td>Poland</td>
<td>11.5</td>
</tr>
<tr>
<td>Portugal</td>
<td>63.4</td>
<td>Hungary</td>
<td>9.4 (253%)</td>
</tr>
<tr>
<td>Netherlands</td>
<td>57.8</td>
<td>Serbia</td>
<td>5.6</td>
</tr>
<tr>
<td>Greece</td>
<td>56.2</td>
<td>Baltic States</td>
<td>4.5</td>
</tr>
<tr>
<td>Spain</td>
<td>52.7</td>
<td>Russia</td>
<td>3.5</td>
</tr>
<tr>
<td>Italy</td>
<td>52.5</td>
<td>Romania</td>
<td>2.8</td>
</tr>
<tr>
<td>United Kingdom</td>
<td>48.7</td>
<td>Bulgaria</td>
<td>1.2</td>
</tr>
<tr>
<td>Slovenia</td>
<td>44.4</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Source – Marketing Research Bureau, IPPC 2010
Does plentiful national plasma supply always deliver equitable patient access?

- Probably yes in countries with high healthcare resources
- Probably no in resource constrained countries unless integrated into national healthcare policies.
- National healthcare budgets therefore remain the dominant constraint and ‘surplus’ donated plasma used for patients in wealthier EU countries.

Is this troublesome??
Sales of anti-D immunoglobulin products per country in Europe in 2008

Use may increase x2 with routine antenatal prophylaxis
Hyperimmune product supply

• Anti D – US dependent and requirement likely to double (routine antenatal prophylaxis)

Europe appears to have exported its ethical and practical Anti- D plasma collection dilemma to the US!!
What are the factors influencing future supply, need and use?

- Healthcare budgets
- Clinical Developments
- Regulation
- Health Technology Assessments
- Manufacturing Economics
Considerations

• > 60% plasma product cost attributable to plasma cost.
• Economics of manufacture/product costs critically dependent on yield.
• Source Plasma availability, price and product price follows market principles and cycles.
• Recovered plasma availability primarily determined by demand for blood components.
• Ideally manufacturers require revenue/sales from at least 3 major products (IVIG, Albumin, Coagulation Factors) to maintain price stability.
Manufacturing economics

Implications

• Increased demand for one product (eg IVIG) may not be met by increased supply unless
  – Price increased
  – Matched by increased demand for other products

• Increased plasma and product supply requires stable/increased global market for all major pd products.

• Interdependency between patient groups for future (increased) access to treatment.

• Increased global manufacturing capacity and supply will be determined by demand for all plasma products.
IVIG no longer treatment for rare diseases – treatment for epidemic – at least in rich countries??

- Need to encourage populations to save for their pensions!
- Also to save and contribute for their future supply of medicines!
- ???A new paradigm
- If it works – then - prophylaxis??
- Yet more demands from ‘baby boom’ generation!!!!
A safe, secure and sustainable supply of plasma products for European patients?

- Should be driven by patient need and demand from healthcare providers and underpinned by evidence based clinical guidelines.
- Should recognise that EU is a culturally, politically and economically diverse region.
- Should promote altruism and recognise the potential relationship and interaction between all forms of donation (plasma, blood, organs, tissues, bone marrow etc).
- Should avoid competition for donors.

BUT

The emerging solution is unlikely to be a ‘binary choice’ between NfP and commercial models for plasma and product supply.
What are the essential components of a European strategy?

• Maximise recovered plasma collection from all countries and where necessary expand source plasma collection – sensitive to local cultural, economic and political preferences.

• Establish EU database on all plasma collection/product supply.

• Supplement ‘competitive market’ with EU strategy for secure supply.

• Ensure ‘surplus’ product available for export.
What are the essential components of a European strategy?? (contd)

- Effective harmonised regulation – sensitive to potential supply implications of precautionary measures eg vCJD recall policies.
- Promote diversified manufacturing capacity and technical innovation in Europe and for Europe.
- Promote development of national treatment protocols and guidelines.
- Ensure strategies safeguard the interests of all patients dependent on the ‘act of donation’ of all substances of human origin. All such acts may be considered as ‘Services of General Economic interest’ and free from normal market and competition considerations.
Should the EU contribute to a global supply – and if so how?

YES

• Maximise recovered plasma collection in all member states
• Support eg WHO programmes to widen regulatory competence and implementation of GMP compliant systems in blood establishments in emerging/developing countries
• Facilitate access to contract manufacturing capacity in Europe through appropriate regulation
• Technology transfer
• Export of surplus products
EU-wide overview of the landscape of blood, blood components and plasma derivatives

Obtain detailed information on the EU landscape of:

- Blood and blood components
- Plasma and plasma derivatives

Provide insight on:

- Main actors involved
- Impact of the growing sector of plasma derivatives on supply and quality aspects
- Efficient utilisation practices