Drivers of Plasma/Blood Donation – Developed Countries

1. 1960’s and 1970’s – ALBUMIN and RED CELLS
2. 1980’s – FACTOR VIII
3. 1990’s to Present – IMMUNOGLOBULIN PRODUCTS

Wide range of patients dependent on a safe and secure supply of blood and plasma products
Global Demand Estimates IVIG

GLOBAL DEMAND FOR POLYVALENT INTRAVENOUS IMMUNE GLOBULIN (IVIG) WITH/WITHOUT ALZHEIMER TREATMENT APPROVAL
2006 - 2016
(Metric Tons)

The Marketing Research Bureau, Inc.
Plasma collected

Product demand

Source: Citi Investment Research

Source: Market Research Bureau
# Immunoglobulin Use in European Countries 2008

<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>Germany</td>
<td>36.4</td>
</tr>
<tr>
<td>Ireland</td>
<td>79.6</td>
<td>Czech Republic</td>
<td>23.2</td>
</tr>
<tr>
<td>France</td>
<td>79.3</td>
<td>Slovakia</td>
<td>19.5</td>
</tr>
<tr>
<td>Austria</td>
<td>78.5</td>
<td>Croatia</td>
<td>13.7</td>
</tr>
<tr>
<td>Denmark</td>
<td>72.8</td>
<td>Poland</td>
<td>11.5</td>
</tr>
<tr>
<td>Finland</td>
<td>70.4</td>
<td>Hungary</td>
<td>9.4</td>
</tr>
<tr>
<td>Portugal</td>
<td>63.4</td>
<td>Serbia</td>
<td>5.6</td>
</tr>
<tr>
<td>Netherlands</td>
<td>57.8</td>
<td>Baltic States</td>
<td>4.5</td>
</tr>
<tr>
<td>Greece</td>
<td>56.2</td>
<td>Russia</td>
<td>3.5</td>
</tr>
<tr>
<td>Spain</td>
<td>52.7</td>
<td>Romania</td>
<td>2.8</td>
</tr>
<tr>
<td>Italy</td>
<td>52.5</td>
<td>Bulgaria</td>
<td>1.2</td>
</tr>
<tr>
<td>United Kingdom</td>
<td>48.7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Slovenia</td>
<td>44.4</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Source – Marketing Research Bureau, IPPC 2010
### IVIG Use - Comparison with Other Regions/Countries 2008

<table>
<thead>
<tr>
<th>Country/Region</th>
<th>Use g/1000 population</th>
</tr>
</thead>
<tbody>
<tr>
<td>•US</td>
<td>120</td>
</tr>
<tr>
<td>•Canada</td>
<td>113</td>
</tr>
<tr>
<td>•Japan</td>
<td>25.9</td>
</tr>
<tr>
<td>•Australia</td>
<td>~100</td>
</tr>
<tr>
<td>•14 Countries of Former EU - Average</td>
<td>55</td>
</tr>
<tr>
<td>•European Average</td>
<td>36.5</td>
</tr>
</tbody>
</table>

- Major differences in clinical practice/IVIG use within EU countries and other countries.
- Best practice guidelines available in many countries eg UK, France, Germany, Australia etc but major variations in demand persist.
- Differences cannot be explained by availability of national GNP/resources – eg Germany is one of the lowest users in the western world.
- SUFFICIENCY OF SUPPLY REQUIRES MANAGEMENT OF DEMAND AS WELL AS SUPPLY.
Japan 2008

<table>
<thead>
<tr>
<th>Fiscal Year</th>
<th>Immunoglobulin derived from domestically collected blood</th>
<th>Self-sufficiency rate(%)</th>
<th>Imported Immunoglobulin</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>1999</td>
<td>2,311</td>
<td>67.9</td>
<td>1,093</td>
<td>3,404</td>
</tr>
<tr>
<td>2000</td>
<td>2,366</td>
<td>67.1</td>
<td>1,157</td>
<td>3,522</td>
</tr>
<tr>
<td>2001</td>
<td>2,982</td>
<td>82.1</td>
<td>649</td>
<td>3,631</td>
</tr>
<tr>
<td>2002</td>
<td>3,125</td>
<td>83.8</td>
<td>606</td>
<td>3,731</td>
</tr>
<tr>
<td>2003</td>
<td>2,937</td>
<td>86.9</td>
<td>442</td>
<td>3,379</td>
</tr>
<tr>
<td>2004</td>
<td>2,984</td>
<td>87.5</td>
<td>426</td>
<td>3,410</td>
</tr>
<tr>
<td>2005</td>
<td>3,097</td>
<td>88.6</td>
<td>400</td>
<td>3,497</td>
</tr>
<tr>
<td>2006</td>
<td>3,210</td>
<td>91.2</td>
<td>310</td>
<td>3,520</td>
</tr>
<tr>
<td>2007</td>
<td>3,266</td>
<td>95.9</td>
<td>140</td>
<td>3,406</td>
</tr>
<tr>
<td>2008</td>
<td>3,347</td>
<td>95.9</td>
<td>144</td>
<td>3,491</td>
</tr>
</tbody>
</table>

Reference: Ministry of Health, Labour and Welfare

* Fiscal Year is from April, 1 to March, 31 next year.
## EU Self Sufficiency??

### EU PLASMA COLLECTION VOLUMES 2007 – Former EU Member States*

<table>
<thead>
<tr>
<th>Population* (Million)</th>
<th>Immunoglobulin Usage (Thousand kg)</th>
<th>Plasma required</th>
<th>Plasma collected 2007</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Million litres @ 4.0g/l yield</td>
<td>Million litres @ 4.3g/l yield</td>
</tr>
<tr>
<td>388</td>
<td>21.3</td>
<td>5.3</td>
<td>5.0</td>
</tr>
<tr>
<td>329</td>
<td>Excluding UK/Ireland</td>
<td>18.1</td>
<td>4.5</td>
</tr>
</tbody>
</table>

* Austria, Belgium, Denmark, Finland, France, Germany, Greece, Ireland, Italy, Luxemburg, Netherlands, Portugal, Spain, Sweden, U.K.

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## EU Self Sufficiency??

<table>
<thead>
<tr>
<th></th>
<th>2007 IgG Self-sufficiency ratio with</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>non-remunerated plasma (excluding UK/Ireland)</td>
</tr>
<tr>
<td>with 4.0 g/l yield</td>
<td>68 % (80%)</td>
</tr>
<tr>
<td>with 4.3 g/l yield</td>
<td>72 % (86%)</td>
</tr>
</tbody>
</table>

*Austria, Belgium, Denmark, Finland, France, Germany, Greece, Ireland, Italy, Luxemburg, Netherlands, Portugal, Spain, Sweden, U.K.*

- Above EU countries are capable of meeting their product needs from locally sourced plasma.
- About 70% of this need can be met from VNRB donations.
- Excluding the UK and Ireland from this analysis because they are unable to use domestically sourced plasma, the remaining 13 countries are capable of meeting between 80% and 86% of their product needs from VNRBD plasma with a surplus from all paid and unpaid plasma used for export to other countries.

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BARRIERS TO GLOBAL SUPPLY

• Cost and affordability
• Plasma supply
• Fractionation Capacity
• ?Regulatory Barriers
Access to Plasma Products - Affordability

Factor VIII usage - WFH Global Survey 2005 (per capita)

- GNP above US$10,000: 3.54 IU
- GNP between US$2000-US$10,000: 0.82 IU
- GNP below US$2,000: 0.02 IU

Note: FVIII on WHO Essential Medicines List
Characteristics of current Supply/Demand Position

- Product follows price
- Not for Profit sector – national focus
- Regulation dominated by US and EU and designed by and for resource rich countries
- Dependency on US plasma supply
- Progressive consolidation of global fractionation industry
- Proprietary technology not available to new players
- Increasingly difficult for eg Developing countries to access contract fractionation for locally collected plasma
Use of recovered plasma in the world
(T. Burnouf, IPFA/APBN Workshop, Kyoto, May 2007)

- 81 million whole blood units = ~ 16 million L recovered plasma
- ~ 3 Million L plasma for transfusion (FFP)
- Of the remaining ~ 13 Million L:
  - ~ 7.2 Million L, mostly from Europe/North America/Japan/Australia, are fractionated
  - ~ 5.8 million L, mostly from ROW countries, are not fractionated - equivalent to 23,200 kg IVIG @4g/litre
Local Plasma Collection and (Contract) Manufacture

• Part of the solution - ‘self sufficiency’ remains an aspirational goal.

**BUT REQUIRES**

• competent national regulatory and technical infrastructure
• organised blood services and quality systems
• access to fractionation capability
• minimum plasma volumes
The ‘Achilles’ project:

A WHO initiative to assure safety and availability of blood products in developing countries

Dr Ana Padilla,
Blood Products & related Biologicals
Essential Medicines and Pharmaceutical Policies Department
Health Services and Systems Cluster
World Health Organization
IPOPI, ISTANBUL OCTOBER 2010
To increase the availability of essential plasma derived products for developing countries by supporting their implementation of national validated quality and safety standards for plasma for fractionation:

- Raising quality standards for production activities in blood establishments
- Providing a framework to make use of, otherwise destroyed plasma, for the fractionation of plasma derivatives
- Using expertise and experience from developed countries

The project includes elements of quality, safety and economical benefits
The “Achilles” project: Expected Outcomes

- Use of local plasma to improve supply of blood derived medicinal products
- Sustainable and affordable blood plasma derived essential medicines
- Increased quality and safety of all blood products in blood establishments
- Optimal use and benefit from donated blood and plasma
- Independent regulatory systems for blood products established
- Potential application of QA and GMP principles to other medical disciplines
- Substantial contribution to public health programs
What can IPFA do?

IPFA Members are primarily nationally focussed organisations reflecting a cultural, ethical and political preference for the VNRBD. But they can:-

- Encourage, support and assist national blood/plasma collection programmes
- Transfer technology
- Support Achilles type projects
- Offer expert support/assistance
- Contribute (?influence) to regulatory decision making
SAFETY vs SUPPLY??

Safety is our top priority
BUT so is supply

• Is there a trade off between safety and supply?
• How do we assess and manage risk? – incremental and often small improvements in blood/plasma product safety carry >> higher cost than other health care interventions.
• Is application of the ‘Precautionary Principle’ always the best solution?
• Does the decision making analysis always take due account of supply?
• Is there any evidence of disproportionate emphasis on safety?
?NO - But Some Barriers to Supply

- Epidemiology
- vCJD Recall Precautions
- Annex 14 of EC GMP Guide
- Regulatory Convergence/Harmonisation – or lack of it!!
- Barriers to market entry – progressive increase in regulatory requirements and cost.
NATIONAL DEMAND MANAGEMENT PLANNING

SUFFICIENCY OF SUPPLY REQUIRES MANAGEMENT OF DEMAND AS WELL AS SUPPLY??

• Can the global market place alone deliver a solution?
• Is demand management simply a form of rationing leading to the creation of ‘death lists’

OR

Sensible approach to use of scarce resource??

• Priority for ID patients and other patient groups for whom there is no alternative treatment
• Need to better understand large differences in clinical use of IVIG between countries with similar GDP’s
Strategies for future secure and safe supply of plasma/products

• Traditional global market models
  – May work for developed countries – but increasing consolidation increases probability of supply failure and its impact!!
  – Product follows price
  – Disadvantages developing countries

• Regional/National Planning for Sufficiency
  – Regional “top-down” strategy
  – National “bottom-up approach” of programmes to achieve sufficiency in source material

• Facilitate access to ‘wasted’ plasma – particularly in developing countries – eg WHO ‘Achilles Project’
Strategies for future secure and safe supply of plasma/products

• Influence global regulatory developments to ensure that supply is not unnecessarily sacrificed for marginal safety improvement.
• Manage and prioritise demand - rationing/optimal use
• Ensure a globally diverse plasma supply and manufacturing capacity – avoid oligopolies
• Strive for some degree of national/regional self reliance in plasma supply
• Plan for the needs of all patients whose lives depend on a safe and secure supply of both blood and plasma products.
Thank You