Safety and Supply of Immunoglobulin Products Outside Europe

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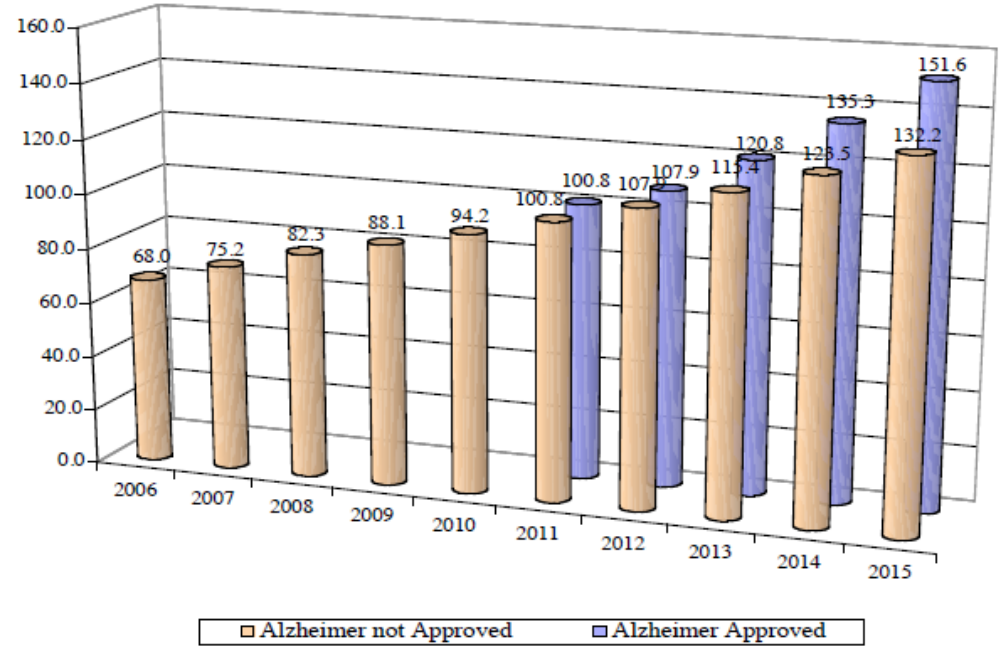
Drivers of Plasma/Blood Donation – Developed Countries

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

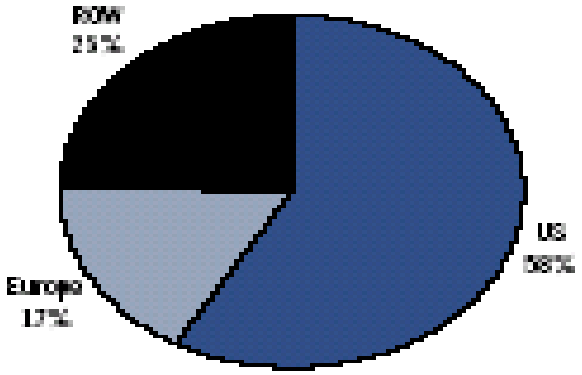
GLOBAL DEMAND FOR POLYVALENT INTRAVENOUS IMMUNE GLOBULIN (IVIG) WITH/WITHOUT ALZHEIMER TREATMENT APPROVAL
2006 - 2016
(Metric Tons)



The Marketing Research Bureau, Inc.

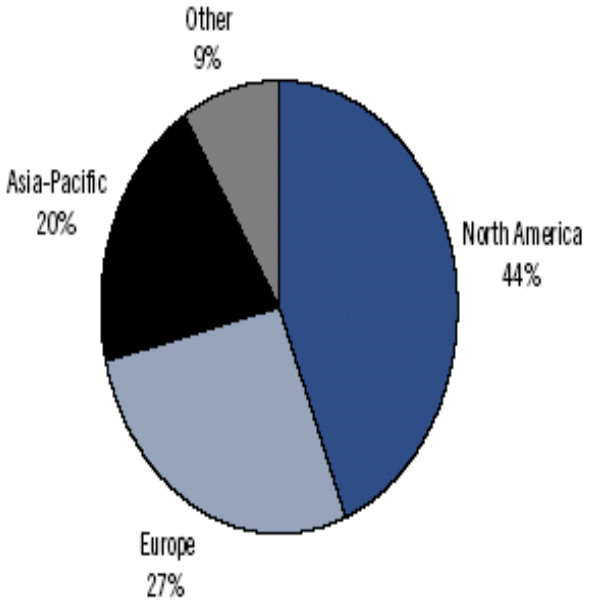
Plasma collected Product demand

Figure 40. Plasma Collection by Region (2008e)



Source: Citi Investment Research

Figure 24. Plasma Derivatives Market by Region



Source: Market Research Bureau

Immunoglobulin Use in European Countries 2008

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

Source – Marketing Research Bureau, IPPC 2010

IVIG Use - Comparison with Other Regions/Countries 2008

Country/Region	Use g/1000 population
•US	120
•Canada	113
•Japan	25.9
•Australia	~100
•14 Countries of Former EU - Average	55
•European Average	36.5

•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

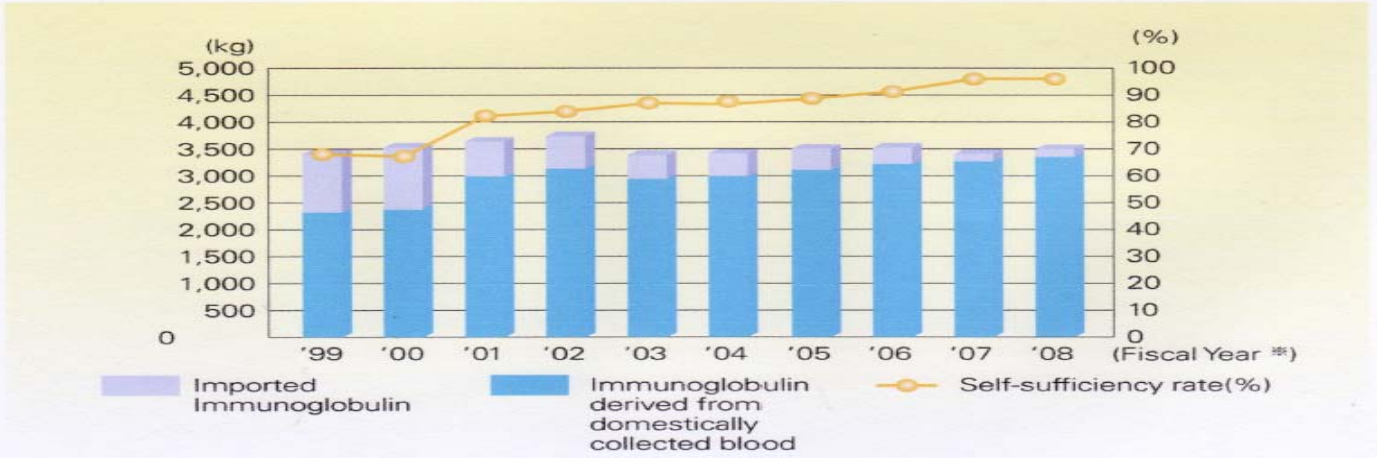
Japan 2008

3-3. Immune Globulin

kg

※ Fiscal Year	Immunoglobulin derived from domestically collected blood	Self-sufficiency rate(%)	Imported Immunoglobulin	Total
1999	2,311	67.9	1,093	3,404
2000	2,365	67.1	1,157	3,522
2001	2,982	82.1	649	3,631
2002	3,125	83.8	606	3,731
2003	2,937	86.9	442	3,379
2004	2,984	87.5	426	3,410
2005	3,097	88.6	400	3,497
2006	3,210	91.2	310	3,520
2007	3,266	95.9	140	3,406
2008	3,347	95.9	144	3,491

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*

Population* (Million)	Immunoglobulin Usage (Thousand kg)	Plasma required		Plasma collected 2007		
		Million litres @ 4.0g/l yield	Million litres @4.3g/l yield	Unpaid Donors (Million litres)	Paid donors (Million litres)	Total (Million litres)
388	21.3	5.3	5.0	3.6	1.5	5.1
329 Excluding UK/Ireland	18.1	4.5	4.2	3.6	1.5	5.1

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

EU Self Sufficiency??

	2007 IgG Self-sufficiency ratio with		
	non-remunerated plasma (excluding UK/Ireland)	remunerated plasma (excluding UK/Ireland)	total plasma (excluding UK/Ireland)
with 4.0 g/l yield	68 % (80%)	28 % (33%)	96 % (113%)
with 4.3 g/l yield	72 % (86%)	30 % (36%)	102 % (122%)

*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.

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

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Health Services and Systems Cluster
World Health Organization

IPOPI, ISTANBUL OCTOBER 2010

The "Achilles" project
Main Goals

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.**


international plasma
fractionation association
Thank You