IPFA, embedded in community

international plasma and fractionation association

Plasma as a Strategic Resource: perspectives and potential solutions in the public sector

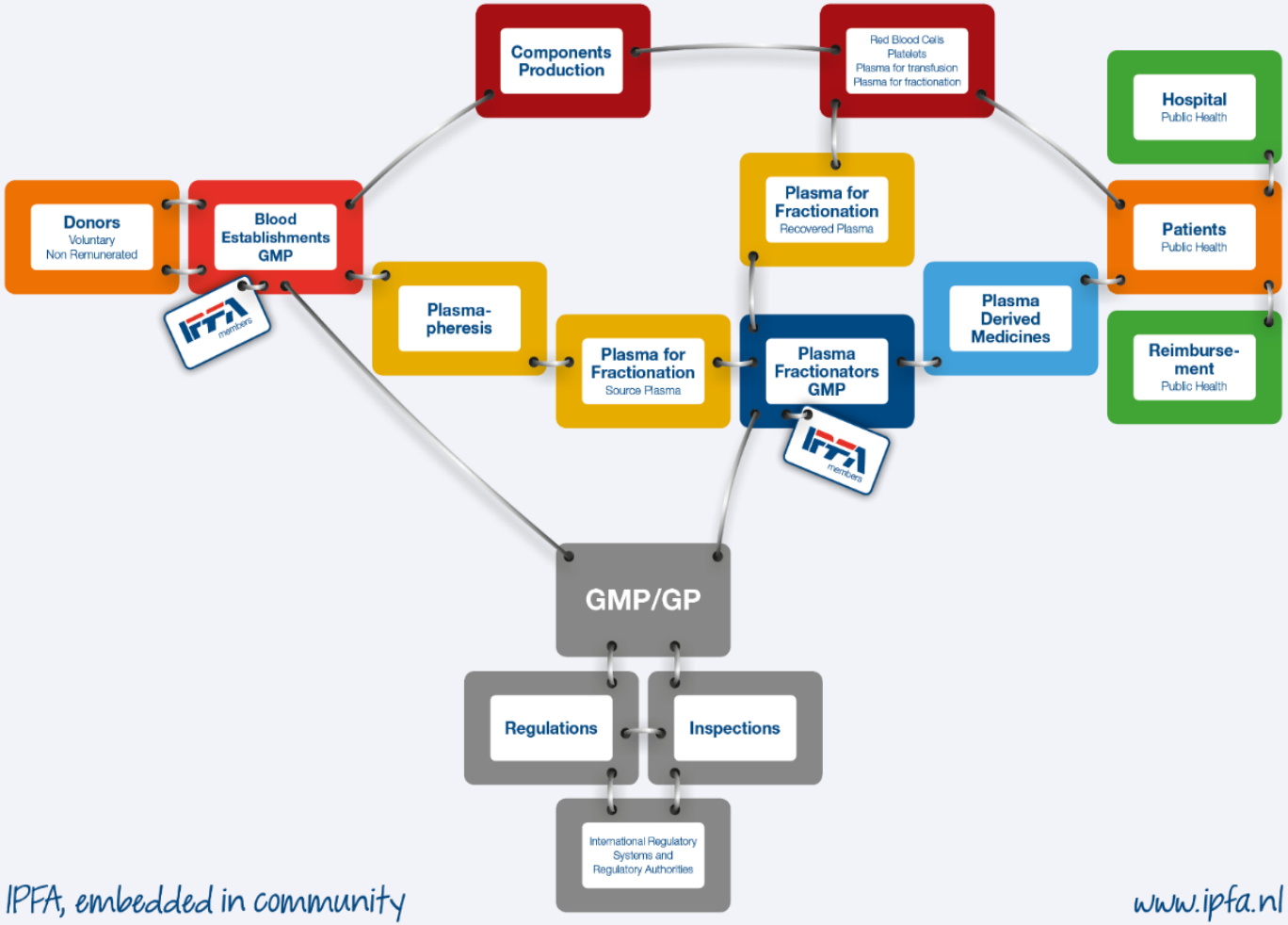
Dr Paul Strengers

Executive Director
International Plasma Fractionation Association

ISdS and IFBDO Conference
"Be there for someone else. Give plasma. Share life"
Rome, Italy
June 15, 2018

Members of IPFA
- not-for-profit plasma suppliers and plasma fractionators -

Bridging the interests of: Donors - Collection Centers - Fractionation Centers - Patients



IPFA's Mission

- An international association for not-for-profit plasma fractionators and national blood services, embedded in community
- Committed to supporting a secure and safe supply of plasma and plasma products
- Promoting a not-for-profit plasma supply from volunary non-remunerated blood donations
- Promoting the fractionation of not-for-profit plasma
- Ensuring greater access to affordable life-saving essential plasma derived medicinal products for patients and health care providers
- Promoting plasma as a strategic resource, by encouraging countries to develop local plasma collections programmes rendering global risks of supply concentration
- Aiming for strategic independence of plasma

Two pillars of IPFA

1. Supply and the quality of plasma

- supply of plasma from whole blood donors (recovered plasma) and plasmapheresis donors (source plasma)
- suppliers of plasma (blood transfusion organizations)
- high quality of plasma for fractionation

2. Plasma fractionation and supply of Plasma Derived Medicinal Products (PDMPs) for patients

- patients and hospitals: high need and demand for plasma products
- expected developments in markets, worldwide

PDMPs have many functions in clinical therapy

- **Replacement therapy:**
  pro- and anti coagulant factor concentrates,
  polyvalent immunoglobulins, specific or hyperimmune immunoglobulins,
  albumin,
  alpha 1-antitrysin,
  C1-esterase inhibitor concentrate.

- **Immune modulating therapy:**
  intravenous immunoglobulin,
  alpha 1 antitrypsin.

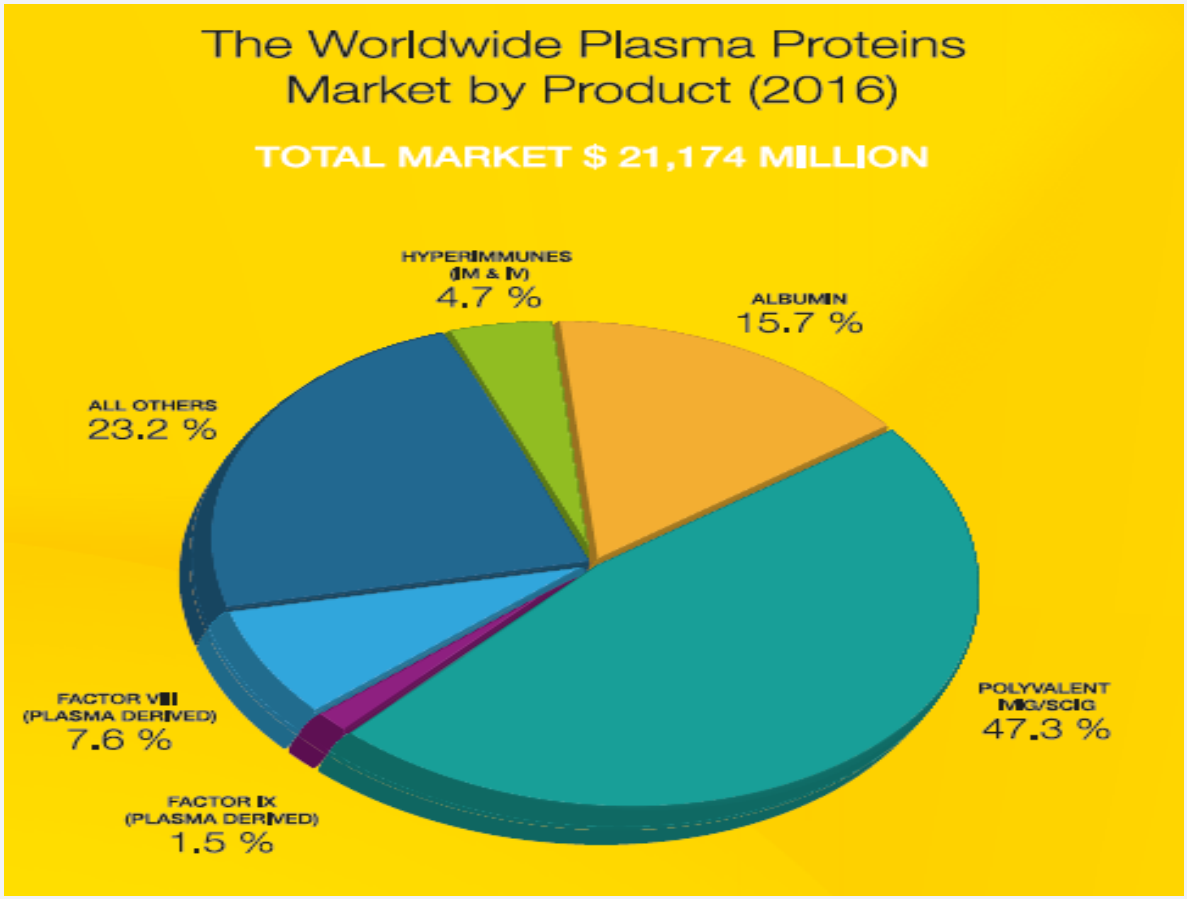
- **Antagonist function:**
  prothrombin complex concentrate,
  activated prothrombin complex concentrate.

- **Anti-inflammation:**
  intravenous immunoglobulin,
  anti-thrombin,
  activated protein C.

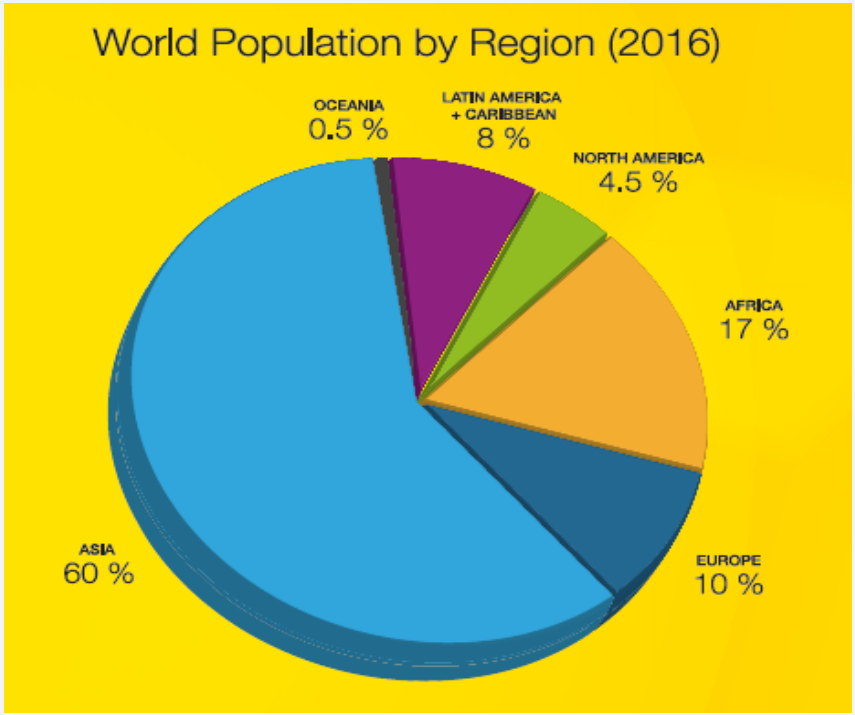
- **Drug delivery:**
  fibrin glue / tissue sealant,
  transferrin

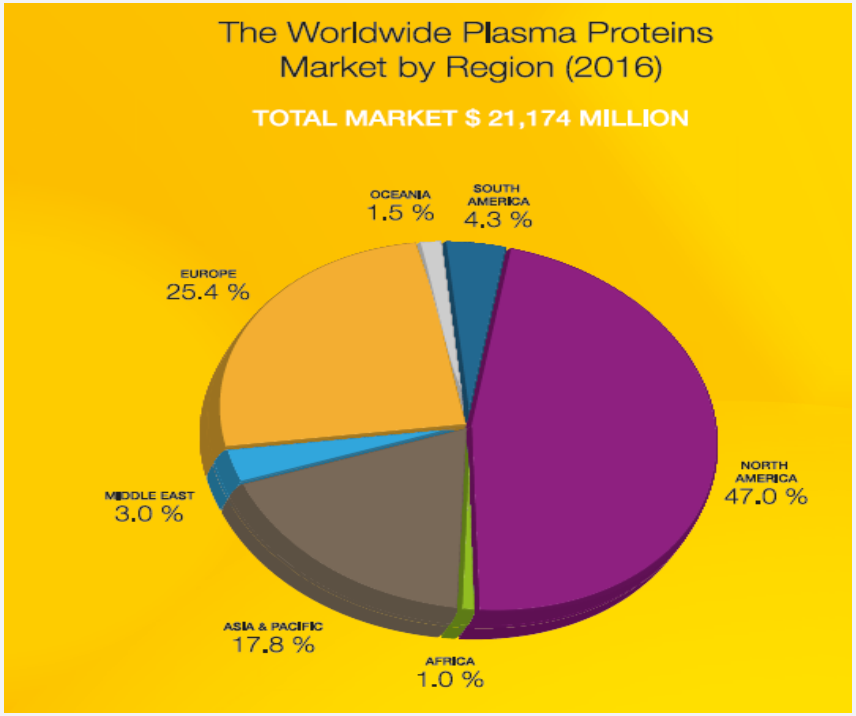
% diagnosed and treated patients worldwide:

- Haemophilia A/B: 30 % and 25% (WFH)
- PID: < 10 % and 6 % (IPOPI)
- AAT deficiency: 10 % and 3 % (AlphaOne)



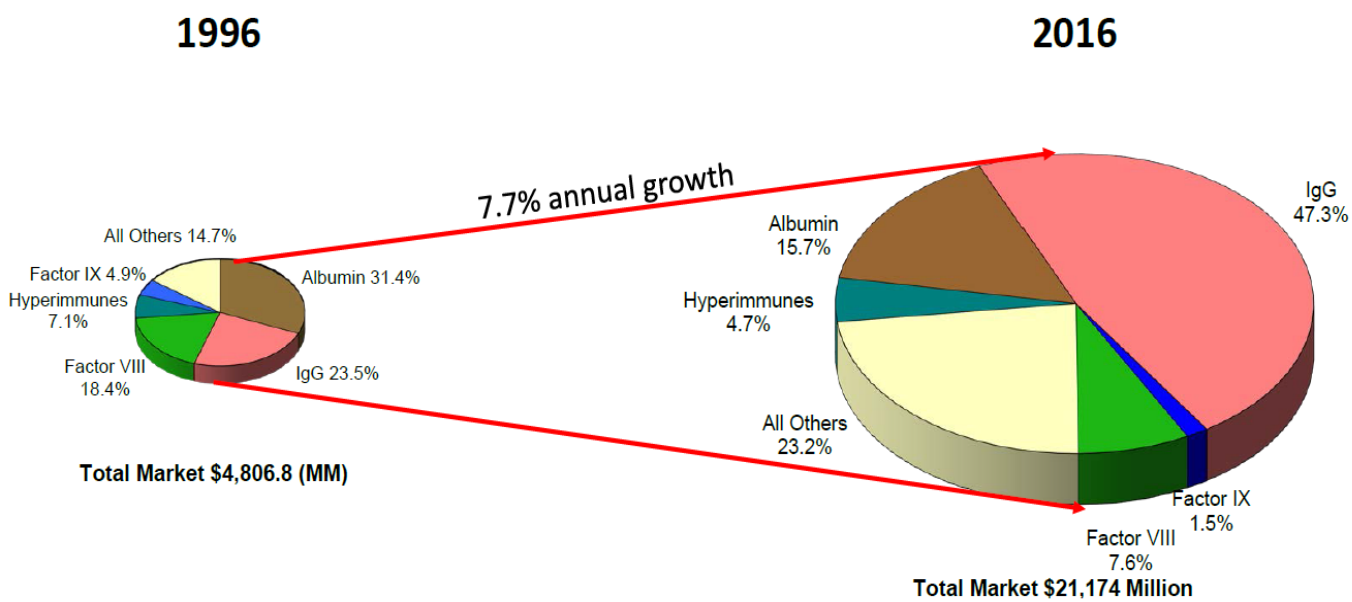
Of the total market, IVIG + SCIG = 47,3%, albumin 15,7%, factor VIII 7,6%





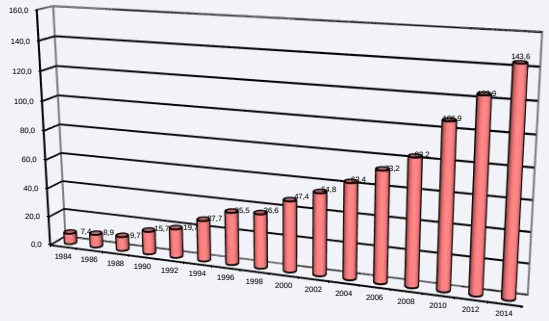
Of the global market, North America holds 47%, but has only 4.5% of the world population,

20 Years of Worldwide Plasma Proteins Market Growth (Without Recombinants)



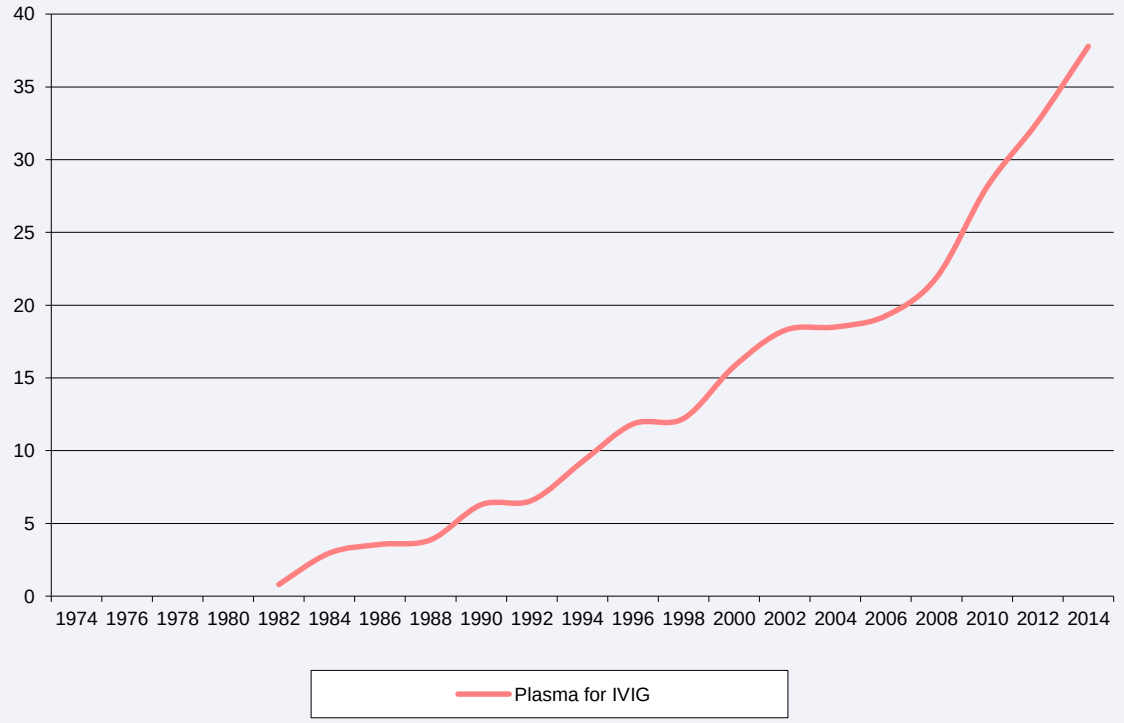
Note: Pie charts are drawn to scale

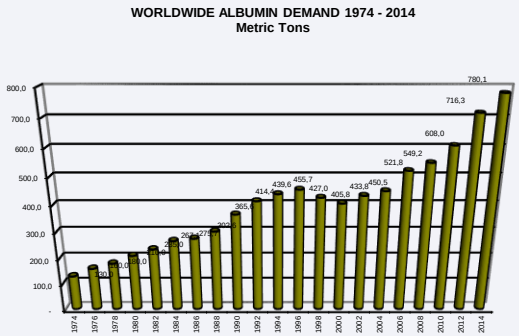
WORLDWIDE DEMAND FOR INTRAVENOUS & SUBCUTANEOUS IMMUNE GLOBULIN (IVIG/SCIG)
1984 - 2014
Metric Tons



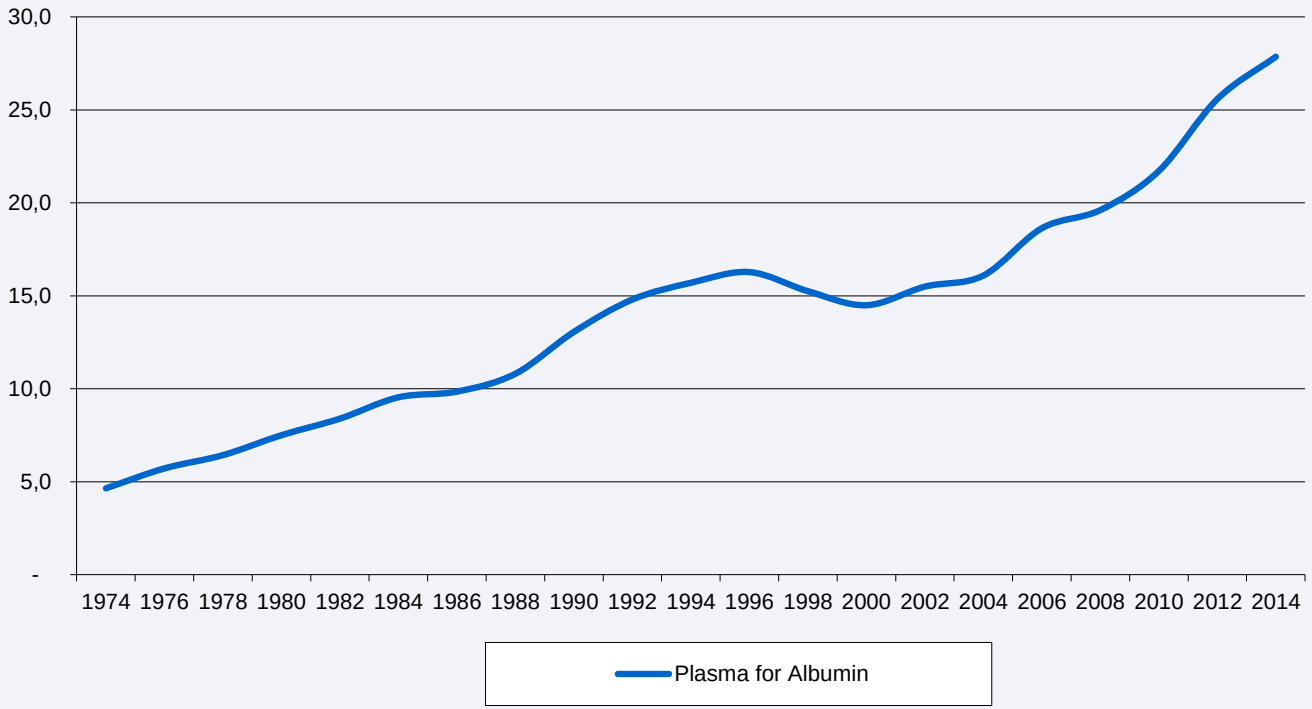
PLASMA REQUIREMENTS FOR ALBU
1974 - 2014 - Million Liters

INTRAVENOUS IMMUNOGLOBULIN

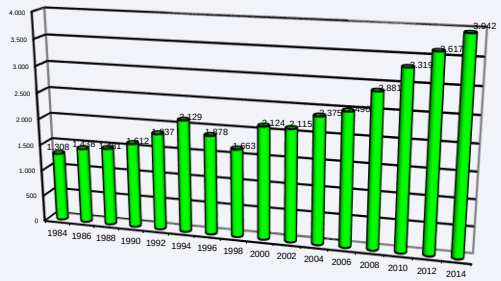




PLASMA REQUIREMENTS FOR ALBUMIN, 1974 - 2014 - Million Liters



WORLDWIDE DEMAND FOR FACTOR VIII 1984 - 2014
Plasma-derived, Million International Units



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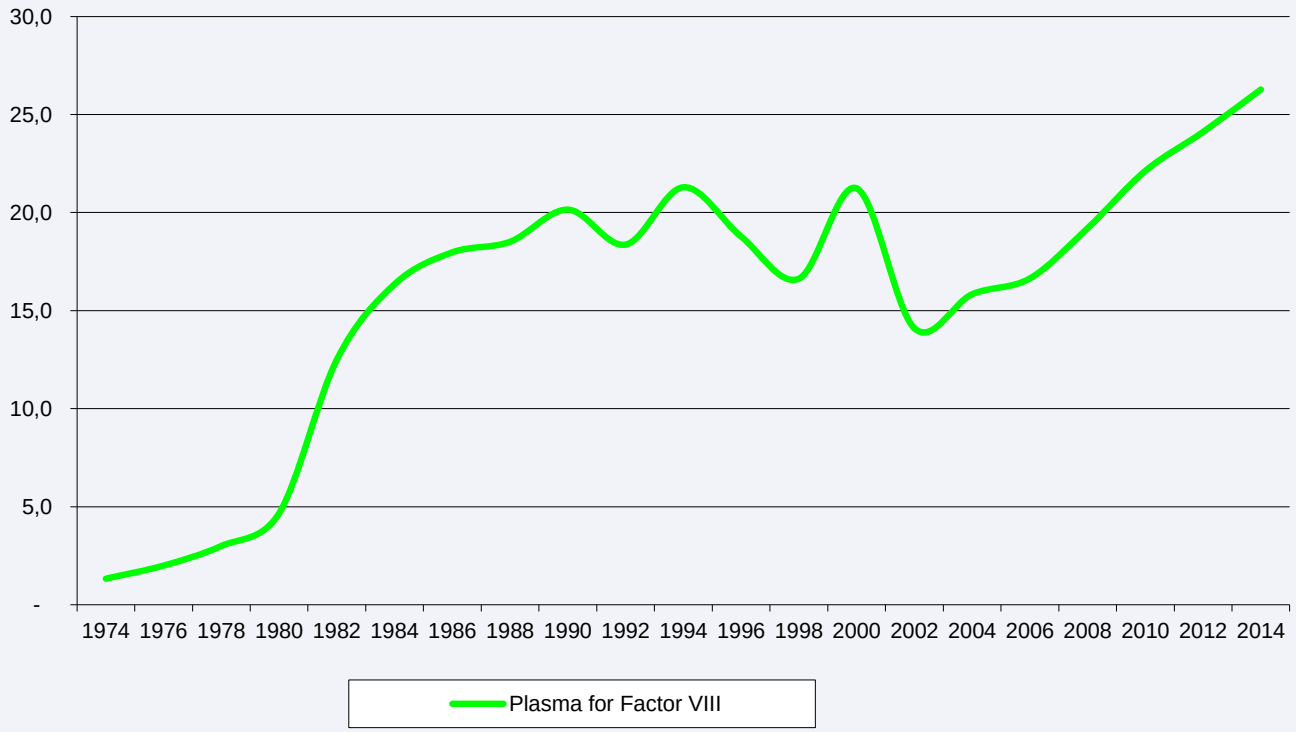
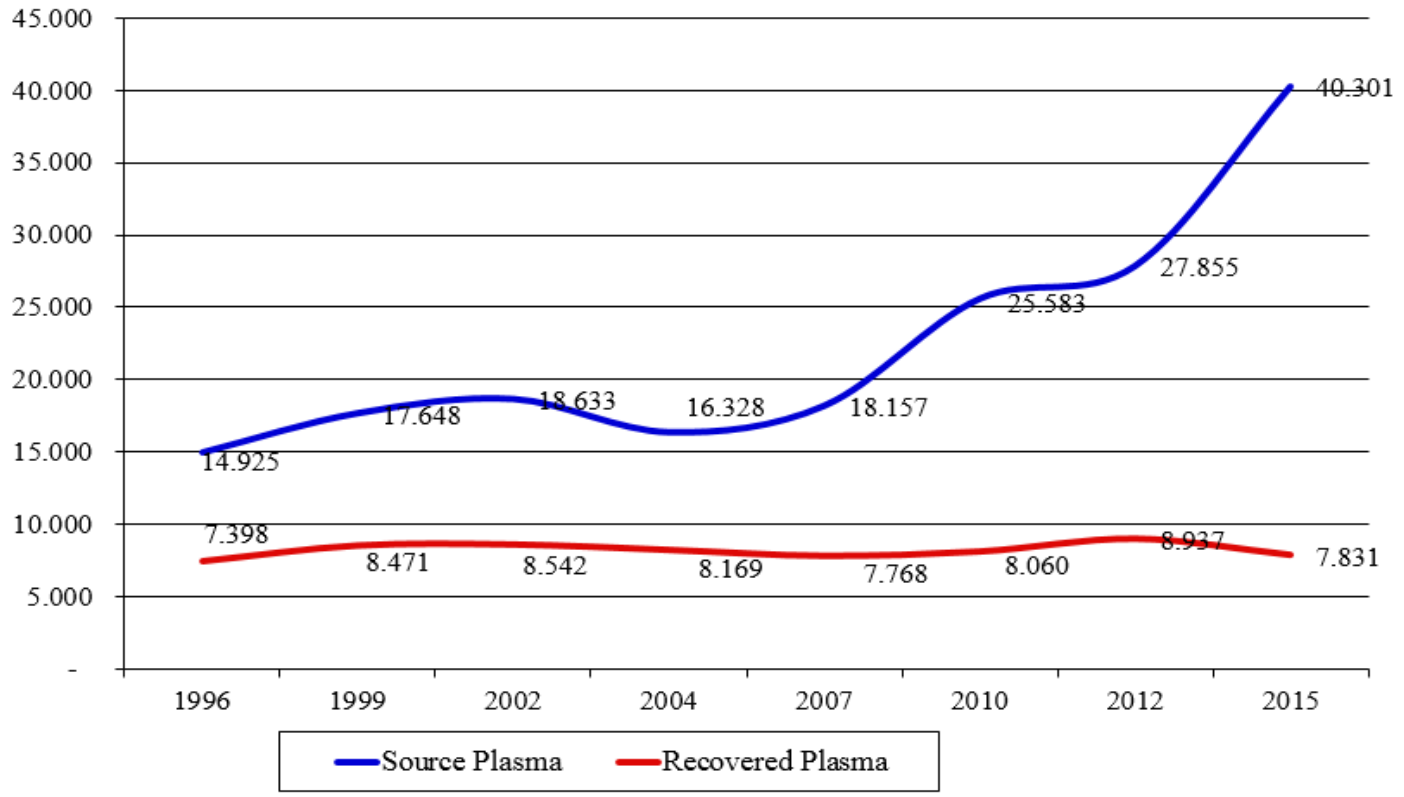
1974 - 2014 - Million Liters

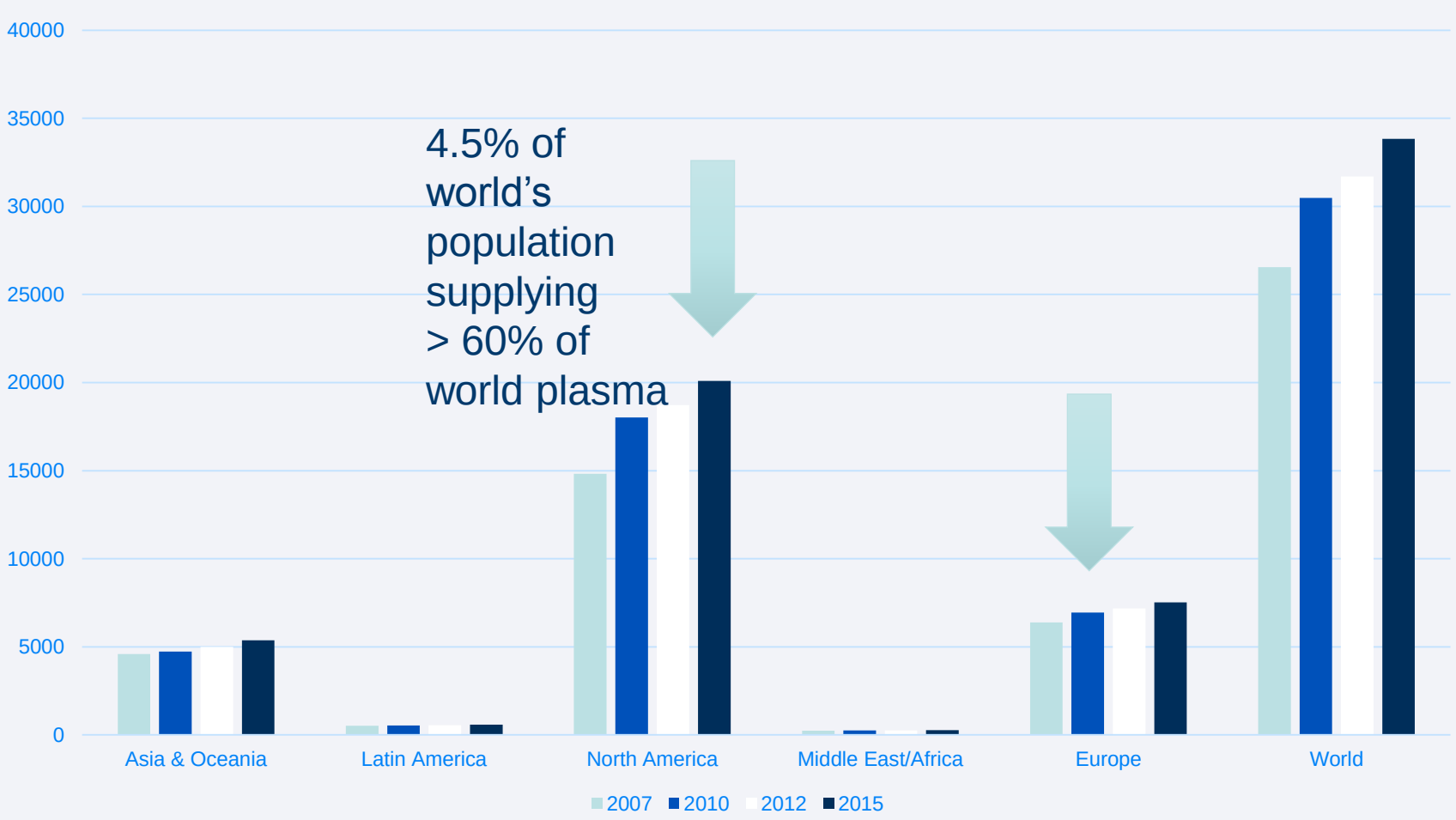


TYPE OF PLASMA FRACTIONATED WORLDWIDE FROM 1996 TO 2015
COMMERCIAL COMPANIES & NON-PROFIT ORGANIZATIONS
(Thousand Liters)
Total in 2015: 48,132,000 Liters



- **Since 2005, the volume of source plasma has more than doubled, while the supply of recovered plasma has remained essentially stable.**
- **> 9.3 million liters of recovered plasma remains unused**

Global plasma supply is out of balance – should we be concerned?



The International Journal of Transfusion Medicine
Vox Sanguinis

ISBT SITS

Vox Sanguinis (2010) **98**, 447–450

DOI: 10.1111/j.1423-0410.2010.01310.x

REPORT

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

B. O. Mahony[1] & A. Turner[2]

[1]*Irish Haemophilia Society, Steering Group PLUS, Cathedral Court, Dublin, Ireland*
[2]*National Blood Authority, Canberra, Australia*

Vox Sanguinis

Received: 14 January 2010,
accepted 14 January 2010,
published online 11 February 2010

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 (IPOPI), the World Federation of Hemophilia (WFH), the European Haemophilia Consortium (EHC), Alfa Europe, Idiopathic Thrombocytopenic Purpura Support Organisation (ITP), Hereditary Angiodema International (HAEI) and Guillain Barre Syndrome Foundation International (GBS/CIDP).

quantity of plasma products required. IPOPI 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.

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Patients, who are dependent on these life-saving therapies, want to be reassured that they will have access to a sufficiënt supply of safe and effective therapy, manufactured from the plasma of carefully selected and tested donors in the future.

60 % of the world' plasma supply comes from only one (1) country.

IPFA's view :

Plasma should be considered as a

Strategic Resource

Strategic Resources are critical materials, defined as :

Economically important raw materials which are subject to a higher risk of supply interruption.

These materials are critical for a region or a country, because their lack of domestic production and / or inability to guarantee national supply through importation.

Examples: drinking water, energy, rare metals, etc.

Source: A Review of National Resource Strategies and Research, March 2012.
http://ww.defra.gov.uk/environment/economy/

Does a higher risk of supply interruption exist?

Examples of interruptions of supply of plasma

- 1980's : HIV (worldwide)
- 1996 : variant Creutzfeldt Jakob Disease (UK, Ireland)
- 2002 : West Nile Virus (La Réunion)
- 2003 : Dengue virus (Puerto Rico)
- 2016 : Zika Virus (Puerto Rico)

Risks for US supply of plasma ?

- For prion diseases
- For non-envelop viruses < 15 nM, no effective pathogen inactivating treatments available

Risk for US supply of PDMPs following interruptions of plasma supply ?

In case of interruptions of US plasma supply:

- Serious consequences for US supply of PDMPs, due to Import restrictions on import of non-US plasma to the US
- **Disasterous consequences for global supplies of PDMPs**

COMMITTEE REPORT

Emerging infectious agents and the nation's blood supply: responding to potential threats in the 21st century

Simone A. Glynn, Michael P. Busch, Roger Y. Dodd, Louis M. Katz, Susan L. Stramer, Harvey G. Klein, Graham Simmons, Steven H. Kleinman, and Susan B. Shurin for the NHLBI Emerging Infectious Disease Task Force convened November 7, 2011

In the early 1990s, the Department of Health and Human Services (DHHS) asked the Institute of Medicine (IOM) to assess how the government, the private sector, and other stakeholders had responded to the human immunodeficiency virus (HIV) epidemic and its impact on blood safety. In its executive summary published in **TRANSFUSION**,[1] the IOM Committee to Study HIV Transmission Through Blood and Blood Products noted that although stakes were high, decisions had to be made under a cloud of uncertainty and that responses were slowed by imprecise and incomplete knowledge, personal and institutional biases, and ultimately by failures in leadership. Emphasizing that blood safety is a shared responsibility, the IOM Committee issued 14 recommendations related to structure and policy including the designation of a Blood Secretary Director by DHHS, the establishment of a Blood Safety Council by the US Public Health Service (PHS), and several recommendations to the Federal agencies involved in the evaluation of an infectious threat, in particular, the Food and Drug Administration (FDA).

Since then, these recomme

Transfusion 2013;53:438-54.

Table 3: EVIDENCE OF TRANSMISSION OF INFECTIOUS AGENTS BY HUMAN BLOOD [9]

INFECTIOUS AGENTS	CELLULAR BLOOD COMPONENTS	PLASMA	PLASMA PRODUCTS
VIRUSES			
HIV I & II	+	+	+
HBV	+	+	+
HCV	+	+	+
Hepatitis Delta virus	+	+	+
HAV	+	+	+
HEV	+	+	+
HGV	+	+	+
TT virus	+	+	+
Parvovirus B19	+	+	+
Human T-cell leukemia virus I & II	+	-	-
Cytomegalovirus	+	-	-
Epstein Barr virus	+	-	-
West Nile virus	+	?	-
Dengue virus	+	?	-
Human Herpes virus-8	?	-	-
Simian foamy virus	?[10]	?	-
Severe Acute Respiratory Syndrome virus	?[11]	?	-
BACTERIA			
Spirochete (syphilis)	+	-	-
Parasites			
Babesia microti	+	-	-
Plasmodium (Malaria)	+	-	-
Leishmania (Leishmaniosis)	+	-	-
Trypanosoma cruzi (Chagas Disease)	+	-	-
UNCONVENTIONAL AGENTS /TSE			
Creutzfeldt Jakob Disease agent	-	-	-
Variant Creutzfeld Jakob Disease agent	+	?	-[12]

+: evidence of transmission; -: no evidence of transmission; ?: questionable or unknown

[9] Most viral transmissions associated to plasma products took place prior to the introduction of efficient viral inactivation or removal procedures

[10] Transmitted by contact with animal blood but not reported by transfusion

[11] Limited epidemiological surveys have not revealed transmission of SARS coronavirus by transfusion but further confirmation may be needed

[12] Investigational studies performed by plasma fractionators using spiked TSE agents indicate that several purification steps used in the manufacture of some plasma products are likely to remove prion agents. These data may not necessarily be extrapolated to clearance of the endogenous form of the TSE agent in human blood.

In 2005:

No Chikungunya
No ZIKA

No MSM donor deferral policies relaxation

No HIV pre-exposure prophylaxis

Source: WHO Recommendations for the production, control and regulation of human plasma for fractionation (2005)
http://www.slideshare.net/rodribera/who-blood-products

Prospects and Risks - Developed Countries

Plasma industry has and will continue to respond to increasing needs for PDMPs. It is in every patient's interest to do so.

BUT

Risk management strategies are needed if this situation continues, and we face :

- **No supply guarantee**
- **Emergence of new TTI in the US, that interrupts the current plasma collections in the US**
- **New clinical indications – resulting in use of IgG for common conditions (eg. Alzheimer's Disease !!)**
- **Trade agreements, market forces, price, currency fluctuations, etc**
- Natural Disasters
- Wars / regional conflicts

IPFA's view for a sustainable system:

1. Plasma is a strategic resource

- Source material for production of essential medicines
- PDMPs are life saving medicines for many patients in many different diseases
- Important for public health (patients and donors)
- High value in public perception
- Great economical value (equipment, tests, capacity, products, etc….)

2. Countries / regions should aim at strategic independence

- Safeguard the supply in a country or a region
- More focus on the supply on source plasma by converting whole blood donors into source donors
- Involvement and commitment of National Blood Transfusion Services
- Involvement and commitment of Authorities (EU Commission, EDQM- Council of Europe, Ministries of Health, policy makers, inspectorates)
- Cooperation of all stakeholders

Strategic Independence for developed and developing countries – What does it mean?

- Develop strategies which mitigate the risks of supply disruption (TTIs, shortages, markets, conflicts etc)
- Reduce supply dependency on one region/country
- Promote and support diverse plasma supply and product manufacture
- Establish appropriate balance between domestic supply and importation
- Establish ‘demand management’ plans

Are there examples of such an approach?

Canadian Strategy

Thursday, May 5, 2016

- Paying donors for the plasma used to make these products is not a safety issue.
- The degree to which we currently rely on the U.S. market makes Canada, and Canadian patients, vulnerable in the event of a disruption in supply. Should no mitigating actions be taken to increase domestic sufficiency in Canada, this risk will become a reality.
- Canadian Blood Services has set a goal to incrementally increase the amount of plasma we collect. Right now, we collect close to 200,000 litres of plasma per year. We will need to collect an additional 400,000 to 500,000 litres per year in the next number of years to diversify our supply and decrease our dependence on foreign sources.

“Canadian Blood Services does not, and will not, pay donors”

Ensuring security of the Canadian plasma supply for Ig

Maintaining the status quo places Canadian patients at risk.

- Submitted business plan to mitigate growing risk to supply of plasma needed to manufacture Ig for Canadian patients to governments in January 2017
  - 50% sufficiency target proposed for Canada
  - Given known risks and potential impacts Ig supply constraints would have on patients, it is important to act swiftly
- Australia and several European countries are similarly making plans to significantly increase plasma collection via public system (Denmark, Belgium, Netherlands, France, Spain and Italy)

Canadian Blood Services
it's in you to give

Graham Sher, IPPC, Budapest 2018

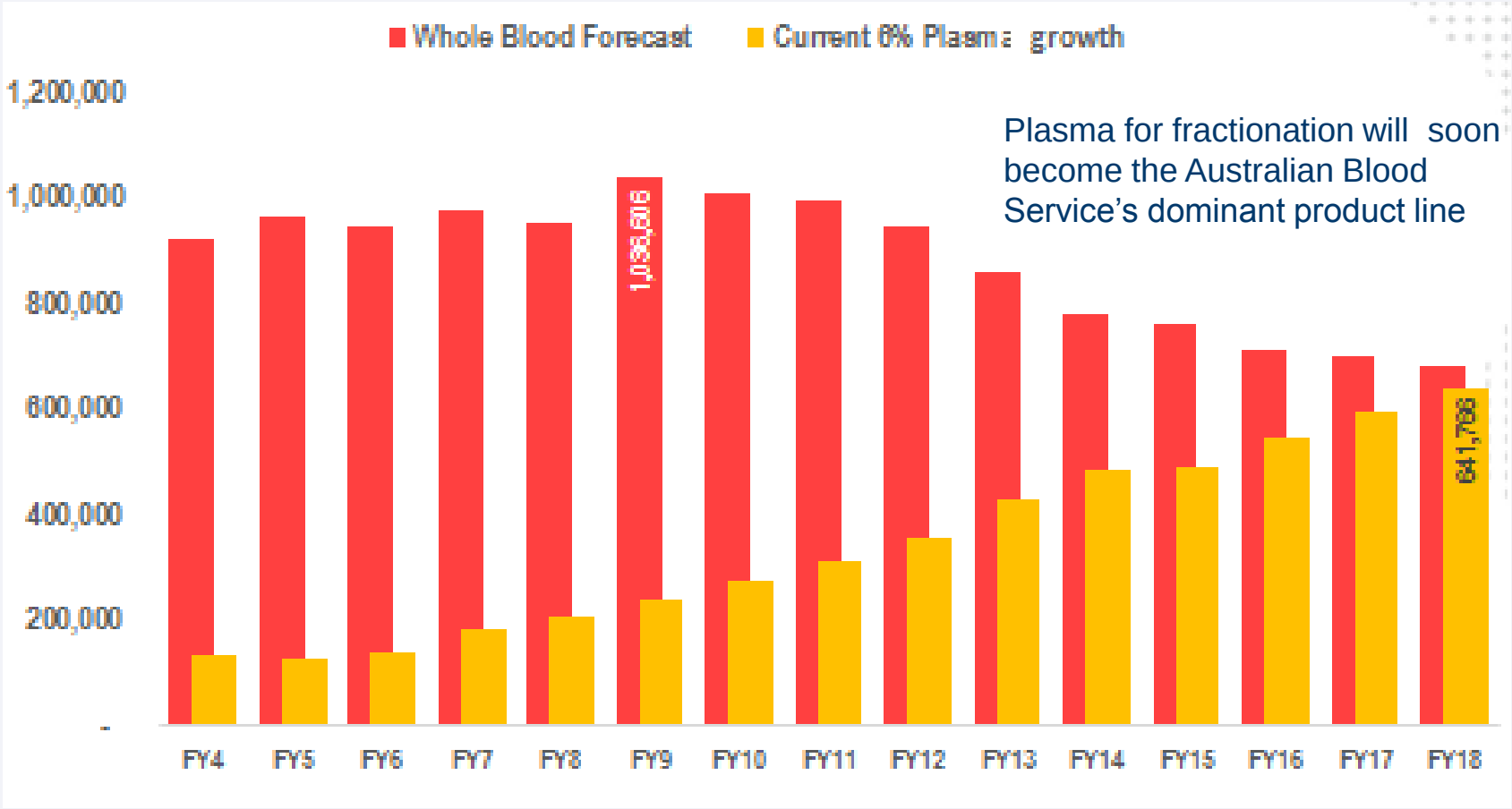
Secure and safe supply of IgG - Australia

Strategies

1. Manage and prioritise Australian demand
2. Reduce cost of collection of plasma
3. Reduce cost of local fractionation
4. Ensure a globally diverse plasma supply and manufacturing capacity
5. Strive for a degree of national self reliance / self sufficiency currently set at 60% of total demand

J. Caulfield, Australia Red Cross Blood Service – IPFA Asia Pacific Workshop. Taipei, March 2016

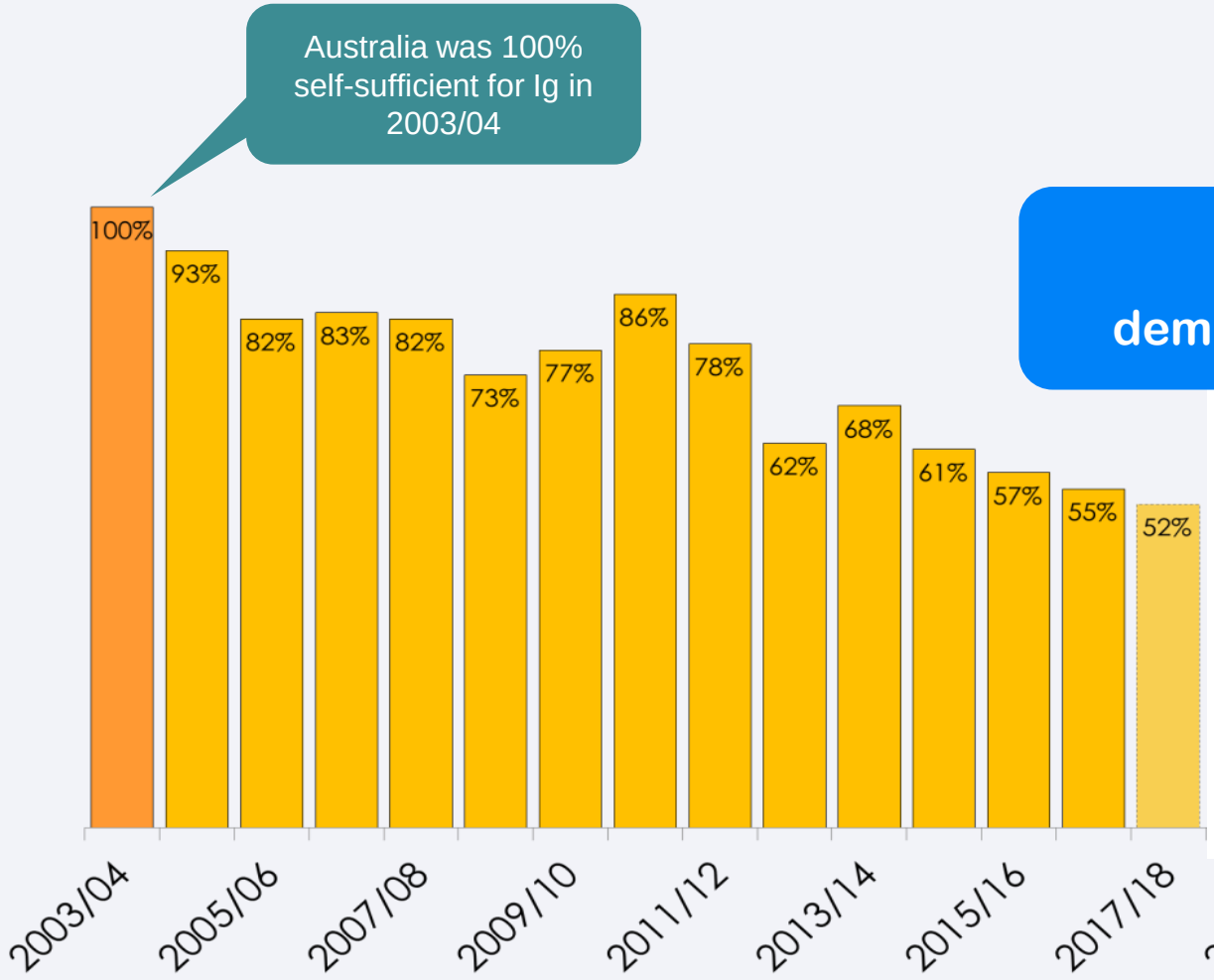
A new paradigm



Plasma for fractionation will soon become the Australian Blood Service's dominant product line

- Change is driven in large part by surging demand for immunoglobulin.
- Australia is one of the highest per capita consumers of immunoglobulin.

Australian sourced Immunoglobulin is not keeping pace with demand growth



11%
demand growth

Demand deficit is mitigated with imported, product, sourced commercially in the US

ABS' Business Strategy

SECURE AUSTRALIAN PLASMA

4 Strategic plasma independence vision for Australia

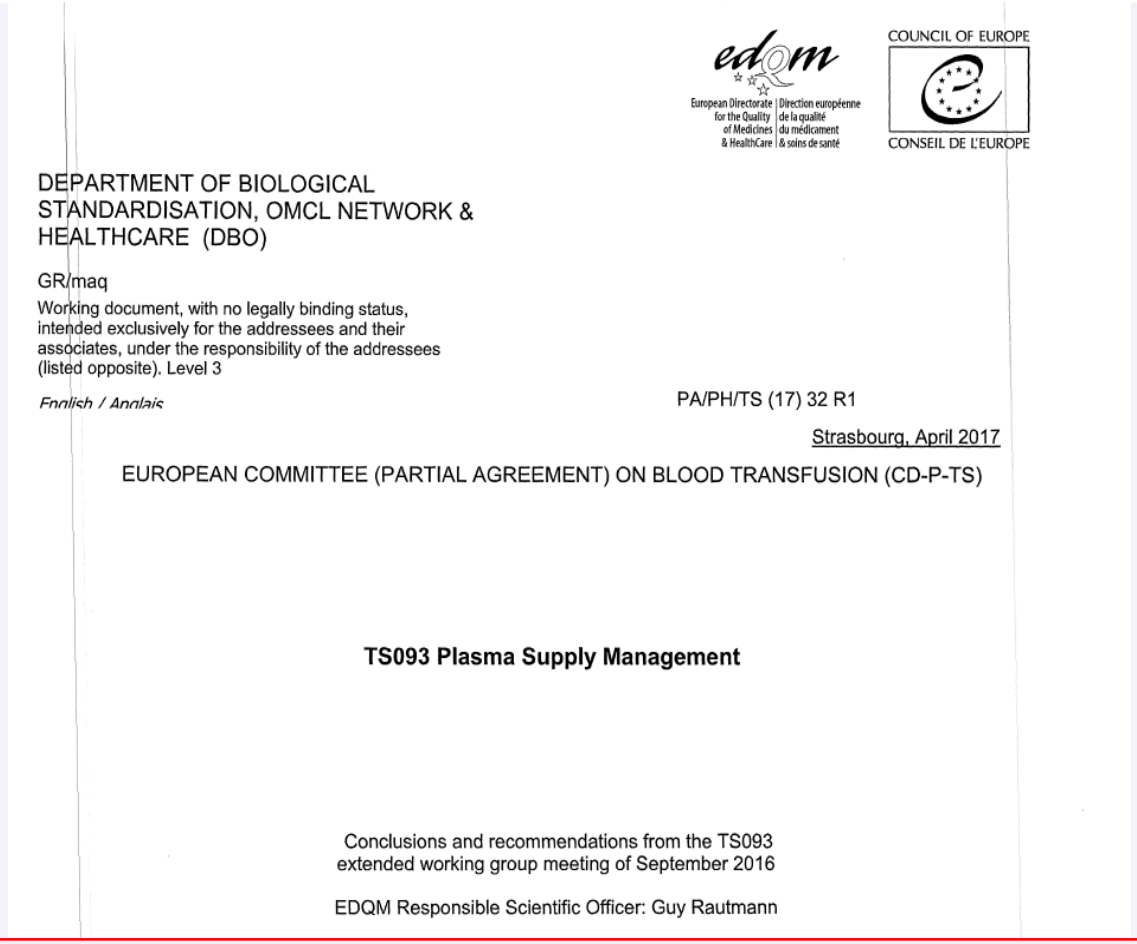
5 Optimise plasma production

6 Build plasma donor capacity for the future

Our Objective:

A manageable, ethical, safe, and affordable level of Ig sufficiency through domestic plasma production to assure **Security of Supply** for Australian patients.

and Europe….?



edqm
European Directorate for the Quality of Medicines & HealthCare | Direction européenne de la qualité du médicament & soins de santé

COUNCIL OF EUROPE
CONSEIL DE L'EUROPE

DEPARTMENT OF BIOLOGICAL STANDARDISATION, OMCL NETWORK & HEALTHCARE (DBO)

GR/maq

Working document, with no legally binding status, intended exclusively for the addressees and their associates, under the responsibility of the addressees (listed opposite). Level 3

English / Anglais

PA/PH/TS (17) 32 R1

Strasbourg, April 2017

EUROPEAN COMMITTEE (PARTIAL AGREEMENT) ON BLOOD TRANSFUSION (CD-P-TS)

TS093 Plasma Supply Management

Conclusions and recommendations from the TS093 extended working group meeting of September 2016

EDQM Responsible Scientific Officer: Guy Rautmann

Recommendations:

scientific meeting on plasma supply management; discussion on VUD and compensation; discussion on IgG levels in healthy persons; description of donorpanels; equipment manufacturers; iron deposit supervision; German regulators on current and coming guidelines.

IPFA's Action Plan 2018-2022

1. Shift from focus on recovered plasma only from VNRBD to promotion of plasmapheresis from VNRBD by IPFA Workshops on Plasmapheresis for educational purposes.

IPFA Global Plasmapheresis Workshop
on Strategic Independence of Plasma
Januari 31st - Februari 1st , 2019, Amsterdam

IPFA Global Plasmapheresis Workshop on Strategic Independence of Plasma

Draft programme

- Facility and logistics
- Economical factors
- Patients depending on plasma derived medicinal products
- Quality and role of competent authorities
- Donor recruitment and social marketing
- Converting whole blood donors into plasma donors
- Donation process, validation of requirements, efficacy, costs
- Immunisation for hyperimmuun plasma
- Donor Safety
- Crowding out of donors

What needs to be done ?

- A balance in global supply of plasma should be established
- Dependency in supply of plasma from only one (1) country should be addressed
- National Blood Transfusion Services should focus on the supply of plasma
- The efficiency of plasma collections and the costs of plasma should be brought in line with the market.
- EU Commission's / National Goverment's supported recruitment programs for plasma donors comparable to organ/tissue donor' programs (Spain, Croatia)
- Countries / Europe should aim for strategic independence of plasma
- **FBDO should assist in converting whole blood donors into plasma donors**

IPFA, embedded in community

international plasma and fractionation association

Thank you for your attention