SESSION 3: PLASMA PROCESSING AND FRACTIONATION

Fractionation in Europe, experience and perspectives IPFA

Dr. Françoise Rossi, International Plasma & Fractionation Association (IPFA), the Netherlands

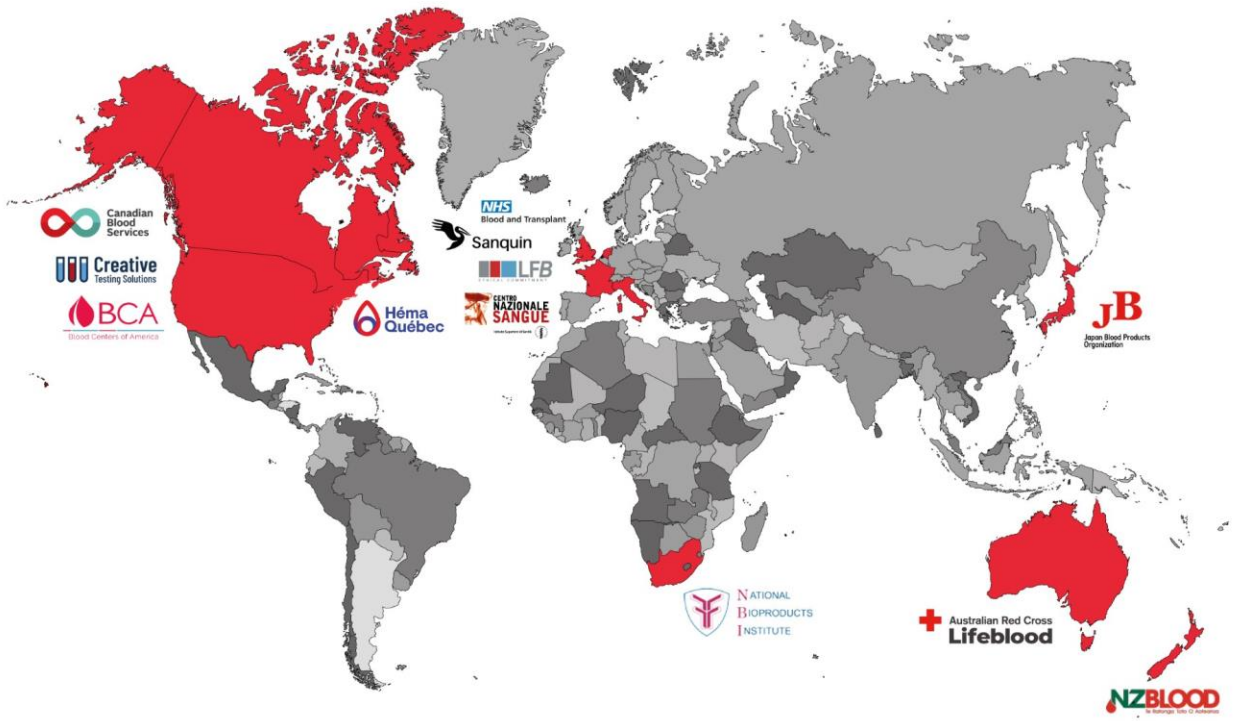
EDQM Stakeholder Event on Plasma Supply Continuity

25-26th March 2025

IPFA, our mission

IPFA supports and promotes the activities of not-for-profit organisations around the globe engaged in the fractionation, collection, and testing of plasma to enable robust, safe supply and patient access to plasma derived medicines.

Through education and collaboration with stakeholders, we advocate for public health values and donor health protection.



Agenda

- European photograph of fractionators - Challenges and Perspectives
- Optimising the use of plasma collected in Europe
- Plasma supply chain models in Europe
- Navigating the regulatory landscape
- Perspectives

Agenda

- European photograph of fractionators - Challenges and Perspectives
- Optimising the use of plasma collected in Europe
- Plasma supply chain models in Europe
- Navigating the regulatory landscape
- Perspectives

European photograph of fractionators

Europe until 1993

Plasma

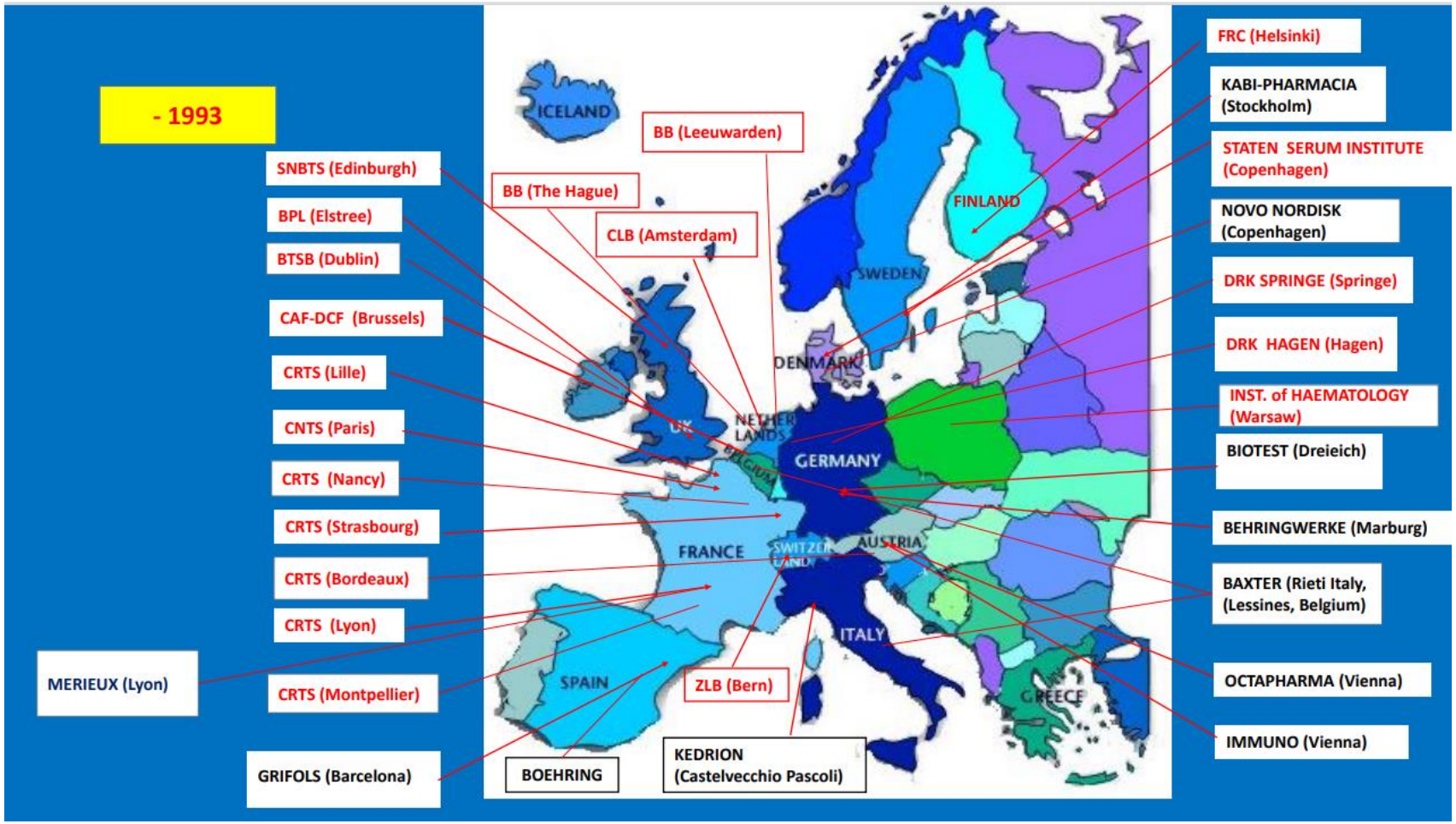
- recovered from local donors

Fractionation

- mainly not-for-profit organisations (BTS): Blood Stable Products (PDMPs)

National environment

National licences + WHO, CoE Guidelines



Adapted from Paul Strengers, EBA/IPFA Joint Workshop, 2022

European photograph of fractionators

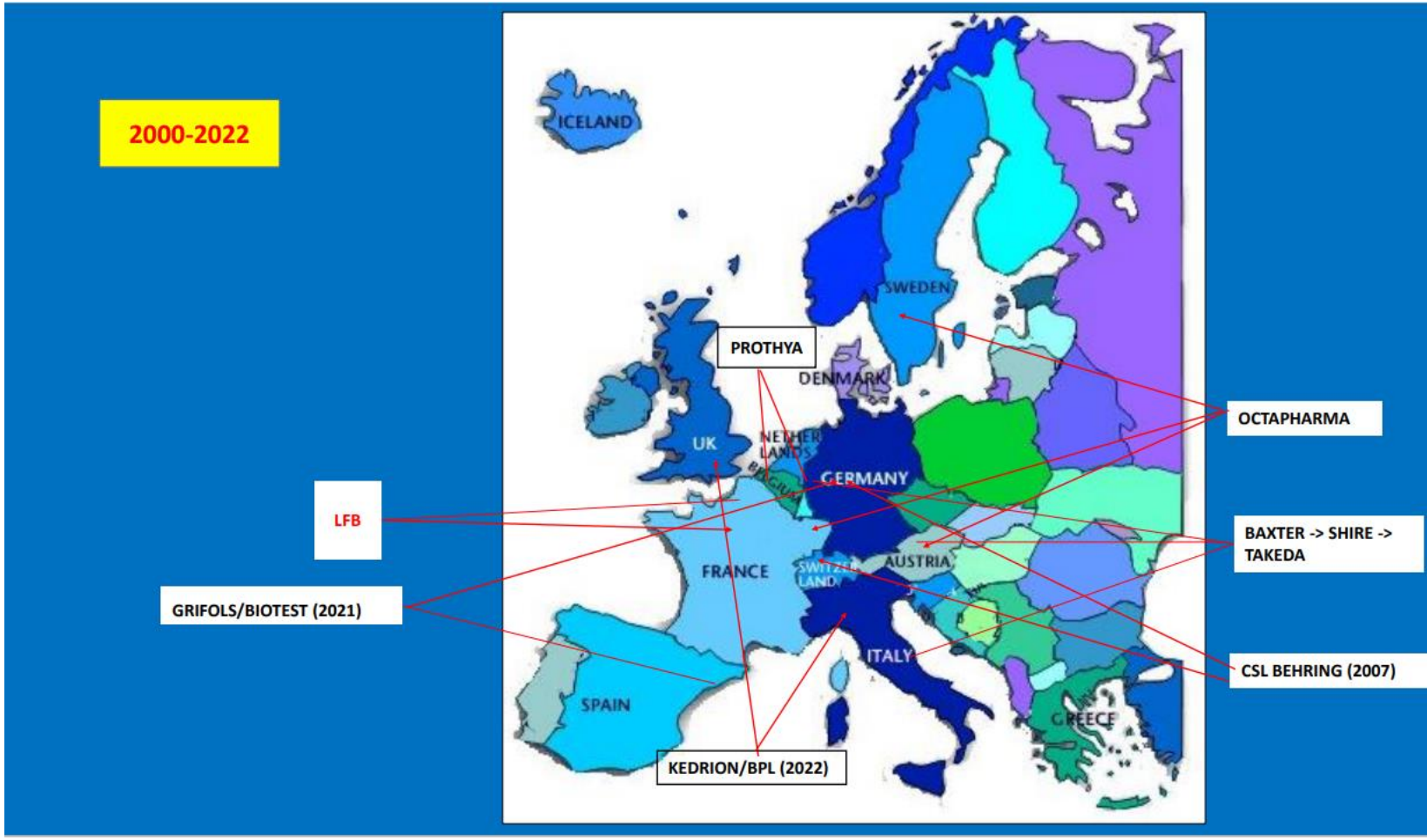
Europe after 1993

- TTI via plasma (paid, from inmates, from VNRBD) ; via PDMPs (factor VIII/IX, IVIG, anti-D IgG)

- Public hearings and court cases (Ireland, Germany, France, Scotland, UK, Switzerland)

➢ **Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use:** Special TITLE X: SPECIAL PROVISIONS ON MEDICINAL PRODUCTS DERIVED FROM HUMAN BLOOD AND PLASMA Article 109/ Article 110

➢ **Directive 2002/98/EC of the European Parliament and of the Council of 27 January 2003 setting standards of quality and safety for the collection, testing, processing, storage and distribution of human blood and blood components and amending Directive 2001/83/EC and daughter directives**



Adapted from Paul Strengers, EBA/IPFA Joint Workshop, 2022

Challenges and Perspectives for fractionators

- **Directive 2001/83/EC – Medicinal Products Directive**

  ⇒ Open EU market for PDMPs => Competition

- **Directive 2002/98/EC – Blood Directives**

  ⇒ Plasma becomes a starting material for PDMPs that can circulate more

  ⇒ Vertical integration of collection in the private sector

Plasma Collection US >> EU
Fractionation EU >> US

- **Regulation (EU) 2024/1938 SoHO Regulation**
- Domestic plasma is a strategic resource = > Plasma for Fractionation becomes a Critical SoHO: Emergency plan

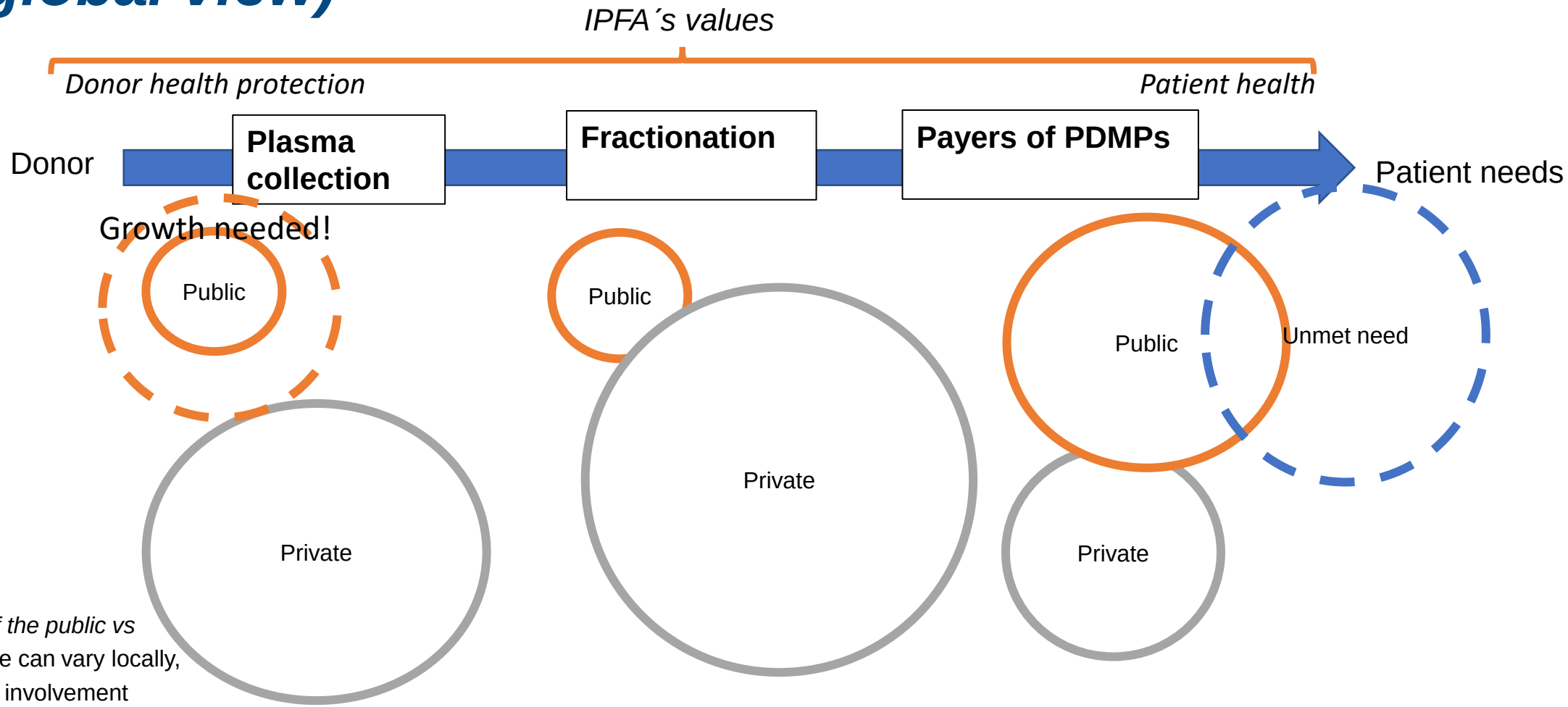
  ⇒ Ideally, plasma collected in the EU returns with the equivalent volume in the form of PDMPs

  ⇒ Contribution in the public health sector => Significant Increase of domestic collections from MS with a Plasma Strategy

- **Steps taken by the Eur. Comm° during the Revision of Blood Directives**

SUPPLY Project - Strengthening plasma collection capacity in Europe co-funded by the European Union's EU4Health Programme that aims to increase and strengthen the resilience of plasma collection in the EU

The role of the public sector in the plasma value chain (global view)



The *proportional size of the public vs private sectors* presence can vary locally, and most times there is involvement of both sectors in parallel

Agenda

- European photograph of fractionators - Challenges and Perspectives
- Optimising the use of plasma collected in Europe
- Plasma supply chain models in Europe
- Navigating the regulatory landscape
- Perspectives

Optimising the use of plasma collected in Europe

SUPPLY

SUPPLY Recommendations - Final

As the project outputs are those of the SUPPLY consortium, they cannot be considered to necessarily reflect the views of any individual organisation which forms part of the consortium.

Co-funded by the European Union

This report is part of the project "101105698/SUPPLY" which has received funding from the European Union's EU4Health Programme (2021-2027). The content of this report represents the views of the author only and is his/her sole responsibility; it can not be considered to reflect the views of the European Commission and/or the European Health and Digital Executive Agency (HaDEA) or any other body of the European Union.
The European Commission and the Agency do not accept any responsibility for use that may be made of the information it contains.

WP3 – Plasma collection and processing best practices

SUPPLY

SUPPLY PROJECT

"Strengthening voluntary non-remunerated plasma collection capacity in Europe"

WP3-T3.2

REPORT ON THE RESULTS OF THE:

"Characterization of the waste of recovered plasma and missed opportunities for plasmapheresis in European Union"

Approximately 2 % of whole blood derived plasma collected in Europe is lost for fractionation due to any reason[xiv], as shown in Figure 16

Figure 16 Proportion of WB plasma oriented to other destinations than transfusion (PfT) and fractionation (PfF), due to all reasons, including destruction in the responding MSs

Optimising the use of plasma collected in Europe

SUPPLY WP3-D3.3

Approximately 2 % of whole blood derived plasma collected in Europe is lost for fractionation due to any reason[xiv], as shown in Figure 16

Figure 16 Proportion of WB plasma oriented to other destinations than transfusion (PfT) and fractionation (PfF), due to all reasons, including destruction in the responding MSs

Technical improvements to increase plasmapheresis plasma for donation collection in Europe

- The type of container may influence the available volume of PfF: plastic bottles would potentially lessen by 2 or 3 % losses observed with bags
- Deaeration of plasma bags: 1 to 5 ml of plasma per bag
- Cryopoor plasma no impact
- Platelet Concentrates Moving from 100% plasma platelet to 30% plasma platelet in some MSs
- Incentives to plasma donors of various natures, including compensation, respecting the financial independence of the donors
- Plasma from First-Time Tested Donors appropriately justified, i.e. in assessing the residual risk to miss positive donations
- Complexity, low knowledge of requirements of plasma for fractionation
- Education and donor management
    - Development of collection in mobile units
    - At frequencies which allow Ig quality and protect donors

Optimising the use of plasma collected in Europe

SUPPLY WP3-D3.3

Approximately 2 % of whole blood derived plasma collected in Europe is lost for fractionation due to any reason[xiv], as shown in Figure 16

Figure 16 Proportion of WB plasma oriented to other destinations than transfusion (PfT) and fractionation (PfF), due to all reasons, including destruction in the responding MSs

Opportunities to increase plasmapheresis plasma for fractionation collection in Europe

- Public European Sector needs to substantially develop its plasmapheresis collection
  - Government pragmatic support needed to start or further develop
  - Implementing actions and regular national campaigns for plasmapheresis donations
  - Lessons learned from the private sector
  - SUPPLY project recommendation and implementation through Field trainings
- Contribution of Ireland and the UK plasma to the EU plasma and PDMP supply Done for UK!
- Standardization of practices
  - Harmonized templates of Quality agreement with fractionators
  - System of accreditation unified at EU level for public sector

  => Mixing of plasma origins would be facilitated
- Investment in plasma collection
- Increasing size of potential volumes available for fractionators in the country, including national centralisation of BEs

➢ Ways to reduce EU dependency to US plasma

Optimising the use of plasma collected in Europe

SUPPLY WP3-D3.3

Approximately 2 % of whole blood derived plasma collected in Europe is lost for fractionation due to any reason[xiv], as shown in Figure 16

Figure 16 Proportion of WB plasma oriented to other destinations than transfusion (PfT) and fractionation (PfF), due to all reasons, including destruction in the responding MSs

Regulatory framework

Simplification and modification of regulatory requirements including

- *Medical staff:* recommendation is that in all EU countries:
  - Donor examination performed by a trained nurse
  - Collection of plasma performed by a trained phlebotomist
  - Physician reached by teleassistance as necessary
- *Active donation-period frequency of plasmapheresis plasma donation* could be raised, always with protection of donor health
- *Volumes of plasmapheresis plasma collected* could be raised, always with protection of donor health
- *Selection of donors/testing criteria* specific donor selection criteria for apheresis PfF should be implemented at national level in all EU MSs
- *Acceptance criteria and testing requirements* => To be revised EDQM Blood Guide and new ECDC guidelines

The value of plasma : Volume and IgG content

WP4- D4.4

Securing commitment and control for the supply of plasma derivatives for public health systems. I & II

•von Bonsdorff, Leni; Farrugia, Albert; Candura, Fabio; O'Leary, Peter; Vesga, Miguel A.; De Angelis, Vincenzo

SUPPLY

TABLE 4 Quality provisions.

Country	Quality agreements in place	Monitoring of IG in plasma	End-user (clinician and patient involvement)
Australia	All agreements follow guidelines set out by the Australian regulator.	Agreement between fractionator and government includes trigger points relating to IG yield. Collector's agreement with the government is based on tonnage supplied for fractionation and includes are performance indicators reflecting IG yield.	Representatives of clinical end-users and patients are included in the Board of the NBA [19]. IG usage is controlled by the Australian Guidelines synthesized by a committee of end-user specialists.
New Zealand	Quality agreements are updated regularly. All NZBS guidelines are approved by the NZ regulator.	The agreement for the manufacture of toll fractionated products reflects indicative yield for IG performance indicators.	Constant interaction with clinical end users to manage demand of IG [36].
Canada	Standard quality requirements are in place with the fractionator.	Contracts stipulate minimum IG yield.	Consulting, meeting and publishing guidelines with clinical end users.
United Kingdom	Standard quality under oversight of the UK regulator.	Fractionator is paid by the gram of IG supplied.	Clinicians involved, patient groups also.
Spain	Uniform quality arrangements across all the BEs in the 17 regions.	IG plasma levels are available. Yields will be specified in the tender relative to a minimum.	Expert committee provides comment and guidance.
Denmark	The tender contract includes agreements on delivery and quality. All BE have to conform Danish blood legislation.	No information plasma IG, yield is specified in the contract conditions.	Representatives from clinical end users participate in wording of the tender.
Italy	Quality agreements are stipulated between the Regional Health Authorities and the fractionator.	A minimum IG yield is specified in the tender specifications. Product over and above this minimum goes back to the consortia.	No.
Portugal	Such agreements are in place. The fractionator conducts audits on fixed sites.	IG manufacturing yield is a key tender criterion and is pegged to levels achieved from the previous tender.	IPST regularly consults all stakeholders when developing tenders and other processes related to its mission.

Abbreviations: BEs, blood establishments; IG, immunoglobulin.

WP3-D3.6

Focus on quality: An assessment of plasma donor characteristics, Immunoglobulin, and Total Protein in donated plasma

IgG/protein concentration has an impact on the yield during fractionation but not on the IgG content and quality of the final PDMPs.

Low frequencies of donations
➔ Higher plasma Ig content
➔ Impacts on production yields

Agenda

- European photograph of fractionators - Challenges and Perspectives
- Optimising the use of plasma collected in Europe
- Plasma supply chain models in Europe
- Navigating the regulatory landscape
- Perspectives

Models for arrangements of plasma and fractionation

ORIGINAL ARTICLE

Vox Sanguinis ISBT International Society of Blood Transfusion

Securing commitment and control for the supply of plasma derivatives for public health systems. II: A survey of national pathways

Leni von Bonsdorff[1] | Albert Farrugia[1,2] | Fabio Candura[3] | Peter O'Leary[4] | Miguel A. Vesga[5] | Vincenzo De Angelis[3]

Vox Sanguinis. 2025;120:124–131.

SUPPLY

Tel +32 2 8806216
info@ supply-project.eu
www.supply-project.eu

Ref. Ares(2023)8290605 - 05/12/2023

C/o BLSI
Clos Chapelle-aux-Champs
30 – bte 1.30.30
B-1200 Brussels
Belgium

WP: 4 Document type: **Position Paper**

Deliverable D4.4:

Position Paper on Distribution of PDMPs coming from EU/national plasma

Domestic Plasma

Domestic Country

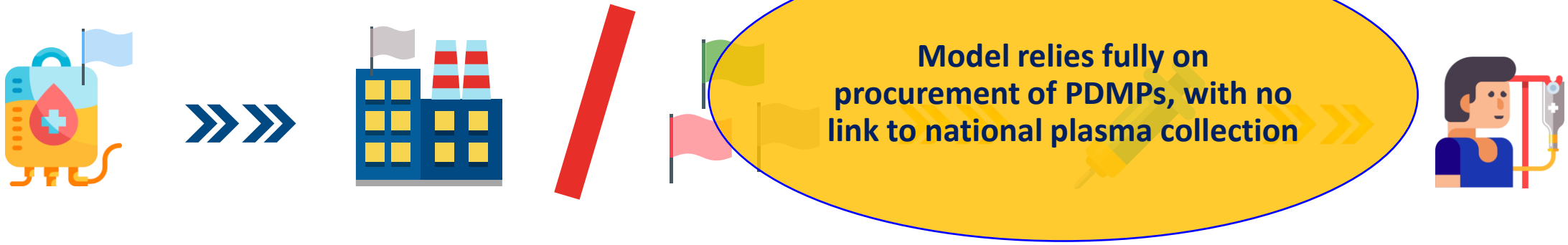
PDMP

Patients within public health care

Other Countries

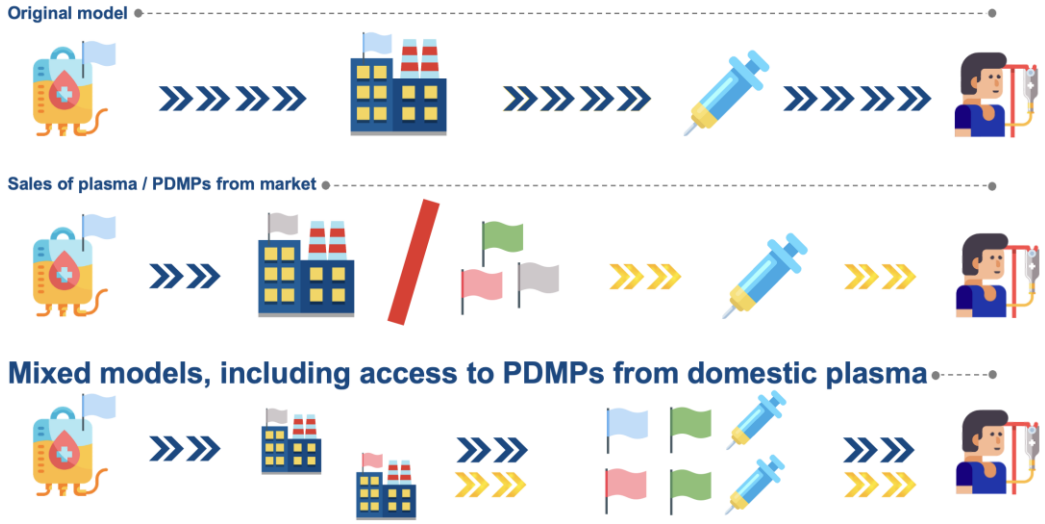
Original model

Sales of plasma / PDMPs from market



Mixed models, including access to PDMPs from domestic plasma

Examples of models in Europe



No European country

Belgium
Denmark
France
Italy
Netherlands
Portugal
Spain
…

Successfully generating PDMPs from publicly sourced plasma requires:

- ***Commitment to support national blood system***
- ***Control by public health authorities in management of arrangements***

Czech R
Finland
Sweden
…

Plasma strategy in some MS: the French mixed model

Plasma collectors and fractionators

Plasma / PDMP national strategy

Government's will of a Plasma/PDMP strategy: Ambition Plasma

- Increase of plasma collection
- Increase of PDMPs production
- National sovereignty
- Plasma Plan: Creation of the Plasma Liaison Committee (Comité Filière Française du Sang)

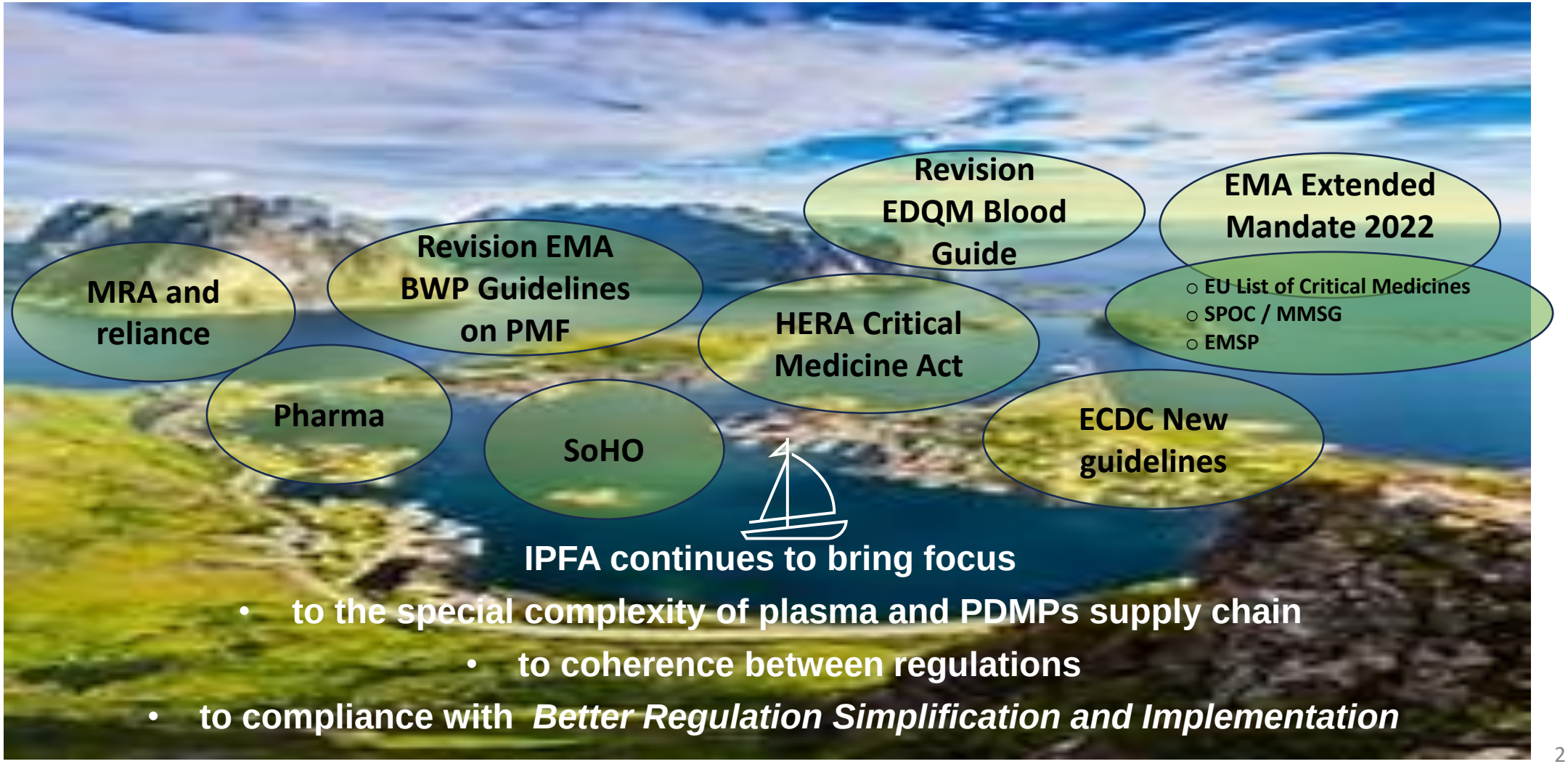
- Cooperation coming from strong long-lasting links with current trust and motivation

- New Local fractionation plant
  - Tripled production capacity; mixed model: local plasma + other sources
  - Started with current production of Ig and Albumin

Agenda

- European photograph of fractionators - Challenges and Perspectives
- Optimising the use of plasma collected in Europe
- Plasma supply chain models in Europe
- Navigating the regulatory landscape
- Perspectives

Navigating the evolving regulatory landscape



Agenda

- European photograph of fractionators - Challenges and Perspectives
- Optimising the use of plasma collected in Europe
- Plasma supply chain models in Europe
- Navigating the regulatory landscape
- Perspectives

Increase in public sector plasma collection is possible

2024 is a record year for plasma: collected over 900 tons

In 2024, 906,938 kilos of plasma were sent to the industry for the production of **plasma-derived medicines**, a figure which represents an increase of 3% compared to the 880,000 delivered in 2023, to which must be added 15,141 kilos destined for the production of Solvent/Detergent virus inactivated plasma. In Italy, **15.4 kilos of plasma** were sent to industrial fractionation for every 1,000 inhabitants (in 2023 this rate stood at 14.9). The objective of 18 kilos per 1,000 inhabitants indicated as the reference value for achieving strategic independence from the foreign market for **immunoglobulins**, the market *driver product*, is therefore approaching

2024 is a record year for plasma: collected over 900 tons

3% increase compared to 2023

Denmark

Blood centres' delivery of plasma has increased from 80 tons (2017) to 124 tons (2023) = 55%
A peak for 2024 indicates a continuing positive development

- Styrelsen for Patientsikkerhed https://stps.dk/nyheder/2023/okt/stor-stigning-i-indsamling-af-plasma-til-fremstilling-af-laegemidler-i-danmark

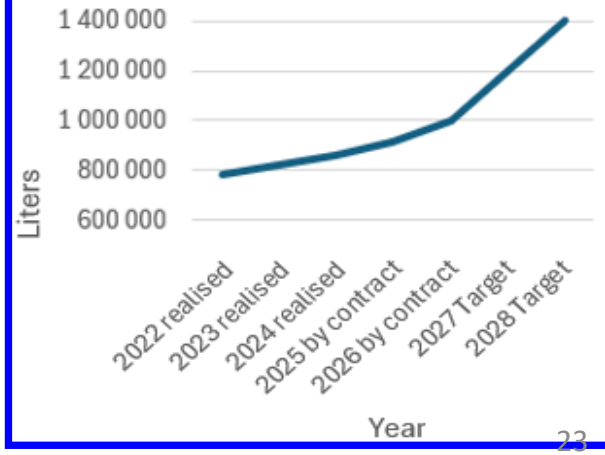
Spain

2024 Significant increase

Belgium Plasma donations 2024: +11.5%

2024: never before have so many plasma collected in Flanders
"In 2024, Belgian Red Cross-Flanders launched a number of campaigns and they clearly worked. In 2024, increased to 160,812 liters of plasma compared to 153,154 liters in 2023. The number of plasma donors also experienced a significant increase with +13.2% donors,"

Plasma Collection France (EFS)



Need for national plasma strategy to increase strategic independence

A **plasma strategy** is an integral part of a country's public health effort.

It is needed to enable robust, safe supply and equitable patient access to life-saving plasma-derived medicines with a sustainable and secure supply of plasma from which they are produced.

By **strengthening the contribution and ability of the public sector** to collect plasma within their communities, and by finding suitable ways to **organize its fractionation**.

Countries and regions can **increase the strategic independence** of these vital medicines in a way which is aligned with wider public health policies and strategies.

Thank you!

For more information about IPFA, please visit our website: www.ipfa.nl or send an email to info@ipfa.nl

PPTA

PLASMA FRACTIONATION IN EUROPE – PERSPECTIVES

Barbara Glantschnig, MSc.
SVP Global Quality
Plasma Operating Unit
26 March 2025

AGENDA

Complexity & challenges of manufacturing of Plasma-Derived Medicinal Products (PDMPs)

Patient need for PDMPs & supply considerations

Safety Standards & innovation

SETTING THE STAGE

The **growing demand for plasma** is driven by two products, **IgG and Albumin.**

More than 70% of the world's plasma supply originates from the United States. Europe depends on it for over 37% of its product needs.

Supply of plasma is facing significant pressure as regulatory hurdles affect collection of more plasma in Europe and the necessary movement of plasma and PDMPs globally.

Costs associated with manufacturing PDMPs are **increasing** (plasma, energy, raw materials, equipment), making it more challenging to invest in new sites, technology and facility upgrades.

Imbalance of global access to PDMPs as cost pressure on HC systems is increasing.

REQUIRED

Stronger stakeholder collaboration and better supply models for sustainable patient access to PDMPs in Europe and globally

PDMP PRODUCTION[1] IS LENGTHY & COMPLEX, REQUIRING UP TO 12 MONTHS FROM DONATION TO DELIVERY TO ENSURE RIGOROUS SAFETY STANDARDS

PLASMA-DERIVED THERAPIES

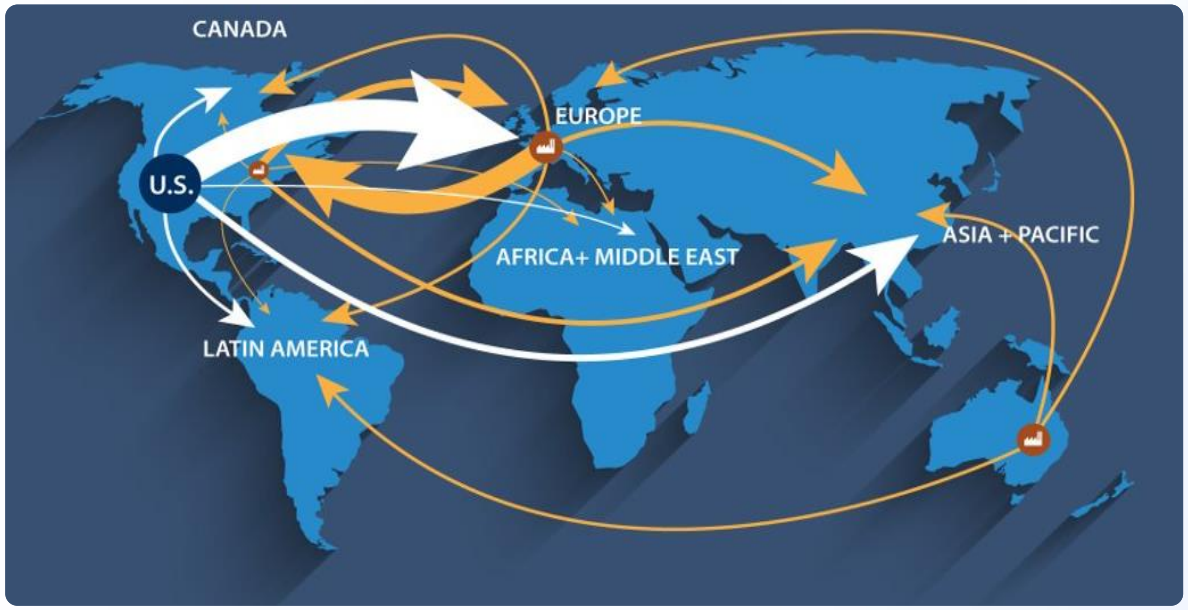
'TRADITIONAL' PHARMACEUTICALS

The production of PDTs is **difficult and time-intensive**, necessitating extensive industrial facilities and specialized, expensive equipment.

Good Manufacturing Practices (GMP) and stringent regulatory standards are followed meticulously at every phase, including thorough testing of both plasma and resulting products, as well as pathogen reduction and inactivation measures.

1) PPTA IQPP and QSEAL
2) PPTA. Uniquely Saving Lives https://assets-global.website-files.com/6397a0a8e779b653e7149a60/6421c0010e3313095fc79c12_10_PDF_EU_SavingLives-inserts_a4_Jan.2023.pdf.

MEETING GROWING PATIENT NEED REQUIRES A GLOBAL PLASMA MANUFACTURING NETWORK SPANNING MULTIPLE CONTINENTS WITH AN INTEGRATED SUPPLY CHAIN



OVER 30 FRACTIONATION PLANTS CLOSED IN THE LAST **40 YEARS**

- Lack of Good Manufacturing Practice (GMP) compliance[1]
- Insufficient volume of plasma or fractionation capacity[1]
- Limited product portfolio capabilities[1]

1. Marketing Research Bureau. Patrick Robert. Plasma Fractionation in Europe current situation and past experience. June 2022.

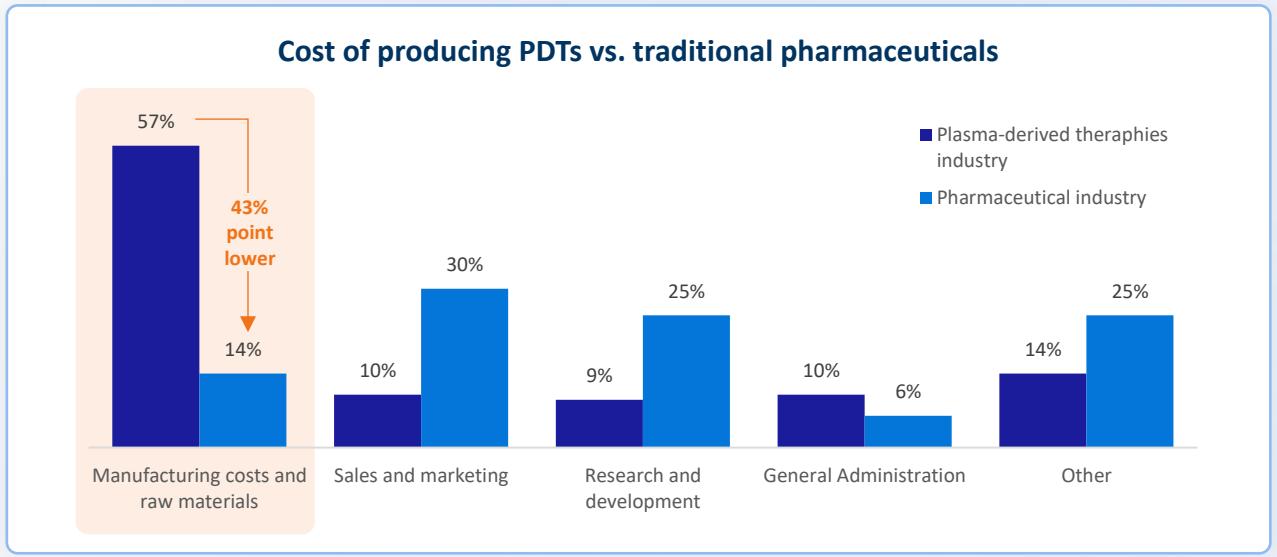
OPERATING IN THE PDMP MARKET HAS HIGH INVESTMENT REQUIREMENTS, LONG PAYBACK PERIODS & PRESENTS DIFFICULTY OFFSETTING PRODUCTION COSTS

PDMP MANUFACTURING REQUIRES HIGH INVESTMENT

Plasma donation center:
~ 3-6 million USD
initial investment

Manufacturing site (end to end):
~ 1-2 billion USD
initial investment

Economy of Scale:
underestimation of complexity and cost of PDMP manufacturing; sustainable models require high volume and a global supply chain

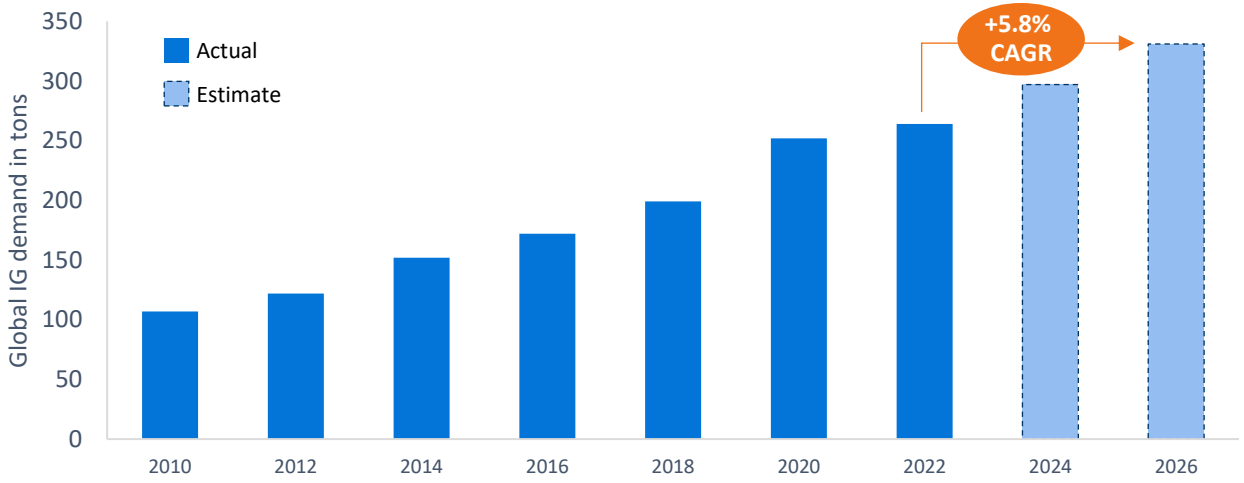


COGS as a percentage of revenue **increased** across the plasma industry on average to **60%+ following COVID,** adding increasing pressure on operational sustainability

PATIENT NEED FOR PDMPs & PLASMA SUPPLY CONSIDERATIONS

PATIENT NEED FOR IMMUNOGLOBULINS, THE FASTEST-GROWING TYPE OF PDMPS, CONTINUES TO RISE RAPIDLY WORLDWIDE, ADDING PRESSURE TO THE SUPPLY CHAIN

The global need for Immunoglobulins will continue to grow at a cumulative annual growth rate of 5-8%[1]



Increasing patient need is being driven by:

- Better diagnosis and patient screening in developed markets[2]
- Improved standards of care in emerging markets[2]
- Broadened use in new disease areas[3], as well as increasing need for treatment of immunodeficiencies and autoimmune conditions

1) Marketing Research Bureau Report, 2021. 2) Chapel H, et al. Front Immunol. 2014;5:627. 3) Berman, K. (2018) Plasma fractionation: The challenge of keeping pace with global Ig demand. Available at: https://www.igliving.com/magazine/articles/IGL_2018-08_AR_Plasma-Fractionation-The-Chellenge-of-Keeping-Pace-with-Global-IG-Demand.pdf.

MORE COUNTRIES AROUND THE WORLD BEGIN CONSIDERING A RANGE OF ACTIONS TO HELP IMPROVE SUSTAINABLE PATIENT ACCESS TO PDMPs

Introducing policies that encourage plasma donation[1,2]

- Using **recovered plasma** from whole blood donations for manufacturing PDTs
- Establishing **plasmapheresis infrastructure**
- Enabling **flexible donation policies** that support both compensated and non-compensated options

Facilitating improved access to plasma therapies

More countries moving to exempt PDMPs from cost containment measures as:

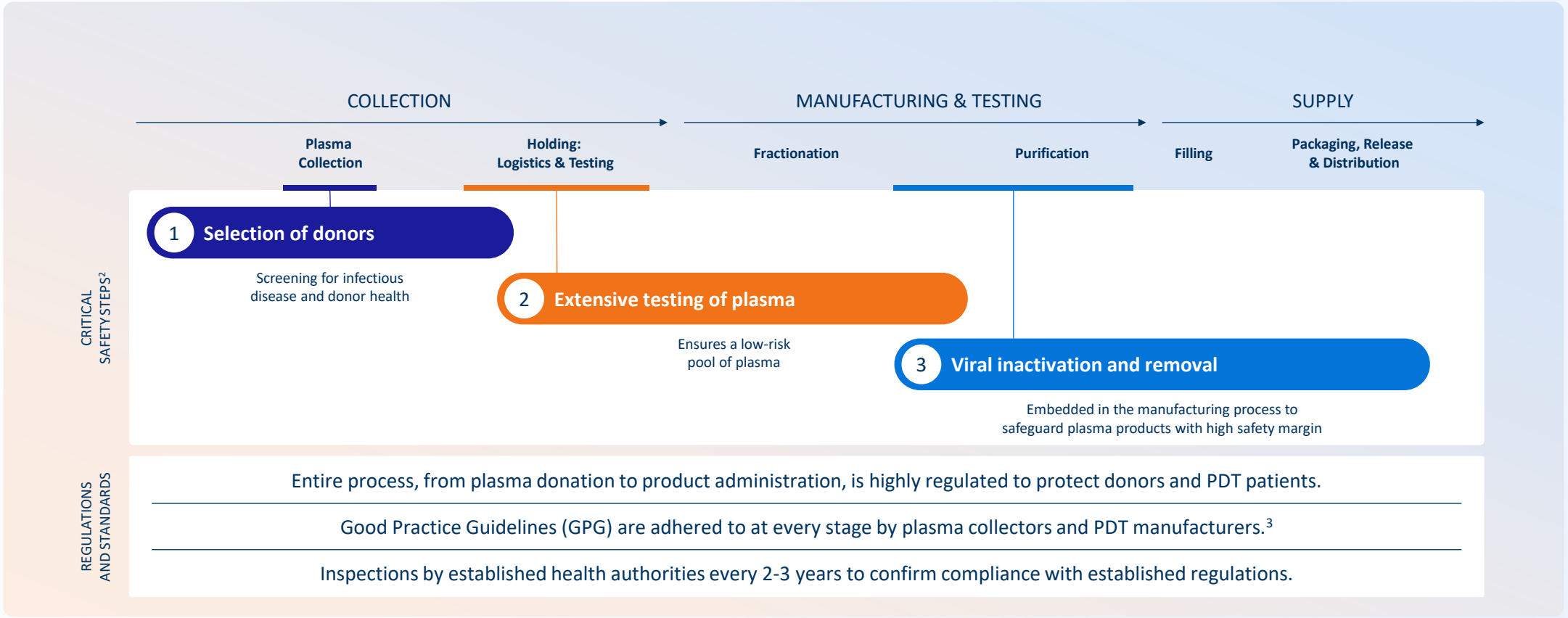
- PDMPs have different cost structures[3]
- Many don't have therapeutic alternatives[4,5]
- WHO lists some as 'Essential Medicines' that should be exempt from tax[6]
- PDMPs are generally used to treat small numbers of patients[7]

Value recognition: PDTs present high clinical and socio-economic value that should be recognized by policymakers and payers[8]

1) PPTA. Together toward a broader European plasma donation ecosystem. https://assets-global.website-files.com/638f893112c6eac0e46ac576/6453f652d7ca1569557512dc_PPTA%20Position%20Paper%20on%20the%20EU%20BTC%20revision_September2021.pdf. 2) IPOPI. PLUS Consensus Principles on Strategies to encourage Blood and Plasma Donations in Europe. https://ipopi.org/wp-content/uploads/2019/02/PLUS-consensus-principles-on-strategies-to-encourage-donations_web.pdf. 3) Marketing Research Bureau. The Plasma Industry. https://marketingresearchbureau.com/the-plasma-industry/ 4) Perez E, et al. J Allergy Clin Immunol. 2017;139(3):s1–s46. 5) Wasserman R, et al. Immunotherapy. 2017;9(12):1035–1050. 6) World Health Organization. Model Lists of Essential Medicines. WHO Model List of Essential Medicines - 23rd list, 2023. 7) PPTA. Who needs Plasma Therapies? https://www.donatingplasma.org/plasma-protein-therapies/who-needs-plasma-therapies. 8) PPTA. Key Economic and Value Considerations for Plasma-Derived Medicinal Products (PDMPs) in Europe. https://www.vintura.com/wp-content/uploads/2020/03/White-paper-key-economic-and-value-considerations-for-plasma-derived-medicinal-products-PDMPs-in-Europe_Vintura-and-PPTA.pdf.

SAFETY STANDARDS & INNOVATION

INDUSTRY HAS MADE HUGE INVESTMENTS[1] IN THE COLLECTION OF PLASMA AND THE MANUFACTURING PROCESS THAT HAVE TRANSFORMED THE SAFETY & QUALITY OF PDMPS



1) PPTA IQPP and QSEAL
2) Kreil TR. Ann Blood. 2018;3:14.
3) Pharmaceutical Inspection Convention Secretariat. 2021.

INDUSTRY IS LEVERAGING DATA, DIGITAL & TECHNOLOGY TO BRING MORE PDMPs TO MORE PATIENTS FASTER, MORE COST-EFFECTIVELY AND MORE SUSTAINABLY

Harnessing data & advanced analytics

Increasing automation and use of robotics

Integrating augmented and virtual reality

Partnering with technology experts

Increasing capacity & yield

Improving process efficiency

Reducing downtime

Enhancing employee safety and experience

Augmenting quality control

Improving productivity

FRACTIONATION → PURIFICATION → FILL, FINISH & RELEASE → PACKAGING & DISTRIBUTION

CONSIDERATIONS TO OPTIMIZE PLASMA FRACTIONATION IN EUROPE FOR A MORE SUSTAINABLE SUPPLY OF PDMPS FOR PATIENTS

WHAT WE NEED

Encourage more donations by adopting science-based donor acceptance criteria for plasma for fractionation, considering risks and established safety margins for PDMPs

Simplify easier import / export regulations for plasma and products to allow optimized use of manufacturing capacities and a global supply model for PDMPs

Fast adoption of novel technologies and automation as well as digital concepts in manufacturing and release of PDMPs (e.g. digital twin models for process simulation)

Accelerated regulatory approval pathways for yield, quality and capacity improvements

“Plasma for Product” as agile and cost-efficient business model to include more countries for plasma supply beyond US and EU (e.g. Asia)

Stronger partnerships between regulators, public health systems, plasma industry and patient organizations

Q&A

PPTA

THANK YOU