

Ways to Avoid Wastage of Plasma for Fractionation from Small Countries

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Disclosures

- *Employee of LFB, in addition to IPFA*

Topics covered in the presentation

Not enough Ig products available in Europe

Not enough plasma for fractionation collected in Europe

Some plasma recovered from whole blood donations
still discarded, in some European Countries, Member States

How to use this plasma for fractionation

Vending/ Contract Manufacturing

What are the needs and main challenges for implementation in
small Countries, MS?

What are the ways to avoid wastage and bring benefit for
small European Countries, MS?

Worldwide use of Plasma for Fractionation

World of plasma for fractionation very diverse: 3 big areas to consider

TRANSFERS OF PLASMA FROM THE U.S. TO OTHER COUNTRIES 2014



EU main supplier of Recovered plasma

- 4,4 ML recovered plasma collected in Europe
 - 58% of PfF in the region
 - 2,9 ML apheresis plasma
- Half of the world recovered plasma for fractionation (from 10% of the world population)

USA main supplier of Source plasma

- ≈16 ML of source plasma collected in USA, used in Europe

Two thirds of the world source plasma
(from 6% of the world population)

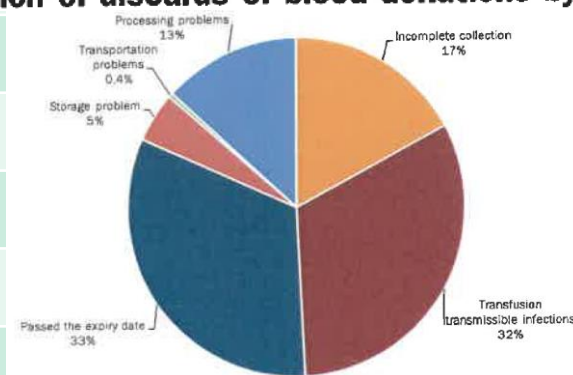
Rest of the world

collected plasma not always compliant with WHO
Quality standards/regulations for fractionation
and any other local applicable regulations
=> large amounts of plasma are wasted

Wastage

WW discard (150 countries)				EU
High income	Upper-middle	Lower-middle	Low income	
48 countries	43	40	19	
5,7%	6,7%	10,9%	9%	EU history of not using PfF

Figure 18. Distribution of discards of blood donations by reason, 2013



Romania

Croatia

Slovenia

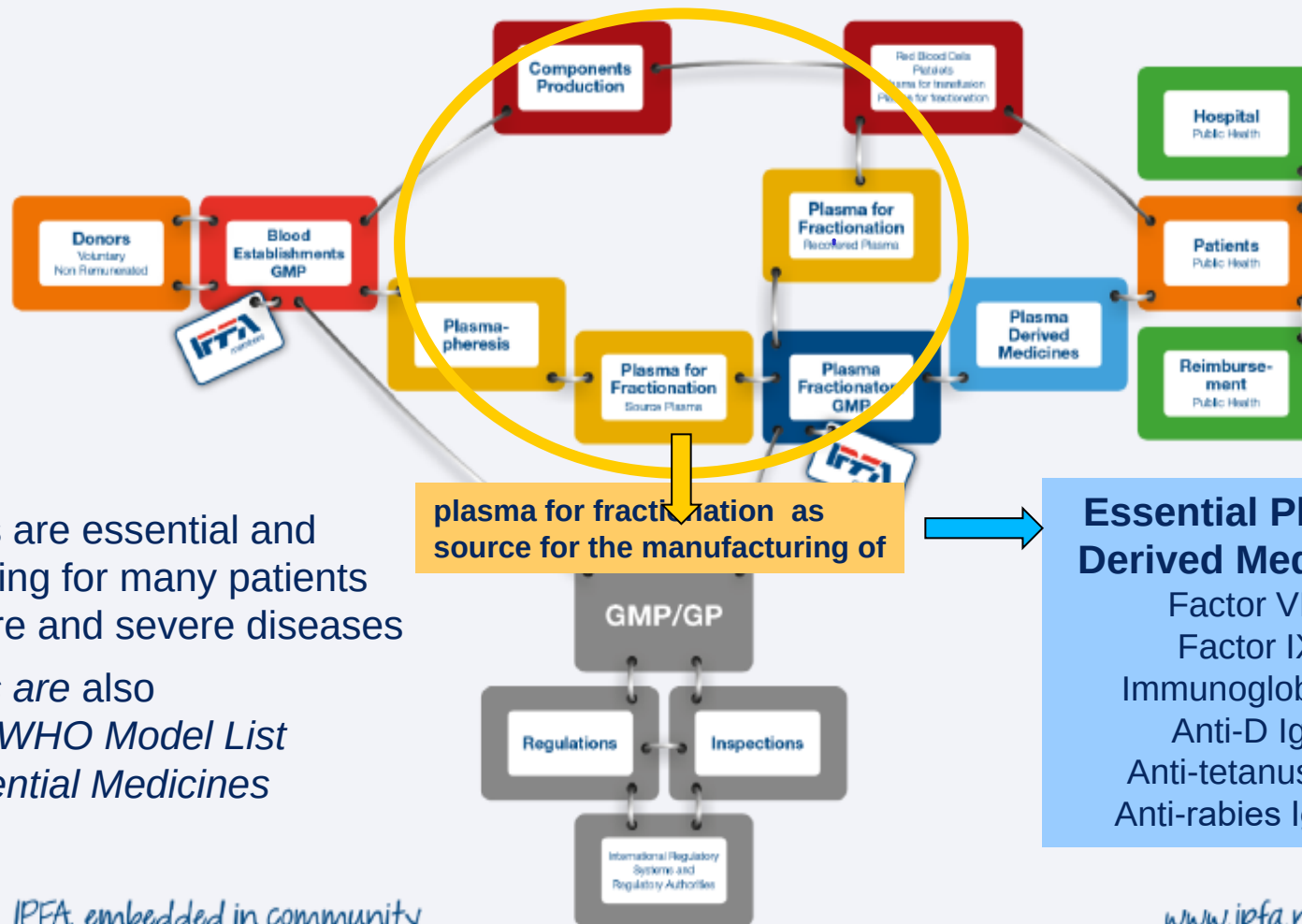
Greece

Portugal

...

- Only 55 of 171 reporting countries produce plasma-derived medicinal products (PDMP) through the fractionation of plasma collected in the reporting country. A total of 90 countries reported that all PDMP are imported, 16 countries reported that no PDMP were used during the reporting period, and 10 countries did not respond to the question.

The Source material for Plasma-Derived Medicinal Products (PdMPs)



Why valuing Plasma PfF?

“PDMPs are in shortage at global level, most severely affecting patients in LMIC.

*Inadequacy of PDMPs in those countries also results from an insufficient domestic supply of plasma of a quality suitable for non-domestic fractionation and from a lack of technical and financial capacity to implement a domestic plasma fractionation programme.” **

- Plasma represents around 30%-45% of the cost of PDMPs

COMMENTARY

Plasma is a strategic resource

Paul EW. Strengers^{1,2} and Harvey G. Klein³
Ref.: *Transfusion* 2016;
56:3133–3137

How to value Plasma PfF?

Common core between Transfusion Products and Plasma for Fractionation

1. Selling/Yielding Plasma to Fractionators

2. Contract Fractionation with a Fractionator

3. Technology transfer from a Fractionator with the aim of ...

4.... Custom Fractionation with a national fractionation(s) plant(s)

Small EU Countries/MS

⇒ In all cases, the story starts the same way:
Availability of sufficient amount of quality PfF

* WHO Guidance on Increasing supplies of plasma-derived medicinal products in low- and middle-income countries 2021

How to do

- 3 Conditions required

- Minimum volume fractionator's requirements

- Volume of plasma for contract fractionation // for vending

from 10'000 L to 50'000 L (in one site)

from 3'000 L

- Increase of plasma (/blood) collection quality
 - Improved by Plasmapheresis plasma
 - Sustainability of BEs

- Meet fractionator/authorities' quality criteria

- Government/ Regulatory authorities' support

Improving access to safe blood products
through local production and technology
transfer in blood establishments



GUIDANCE ON INCREASING SUPPLIES
OF PLASMA-DERIVED MEDICINAL
PRODUCTS IN LOW- AND
MIDDLE-INCOME COUNTRIES
THROUGH FRACTIONATION OF
DOMESTIC PLASMA

World Health
Organization

Critical parameters for insuring quality of Plasma PfF

= Acceptance Criteria by the Fractionator

Quality management; Develop a culture of quality in BEs

Good Practices Guidelines

for Blood Establishment Required to comply with Directive 2005/62/EC
Per Commission **Directive (EU) 2016/1214** (in force 15/02/2018)

- *only 84% of EU countries have national Quality assurance and monitoring system*
- *only 83% of EU countries have haemovigilance system*

Chap 5: STANDARDS AND QUALITY MANAGEMENT IN BLOOD ESTABLISHMENTS

- 5.1 Standards for donor selection
- 5.2 Standards for quality-assured laboratory testing for evidence of transfusion-transmissible infection
- 5.3 Good manufacturing practices (GMP) and quality management
 - 5.3.1 Suitable organization and trained personnel
 - 5.3.2 Suitable facility and equipment
 - 5.3.3 System of documentation and traceability
 - 5.3.4 Validation of operating procedures and quality monitoring
- Traceability of plasma units and blood monitoring system (look-back management) (haemovigilance and pharmacovigilance)



WHO Guidance on Increasing supplies of plasma-derived medicinal products in low- and middle-income countries 2021

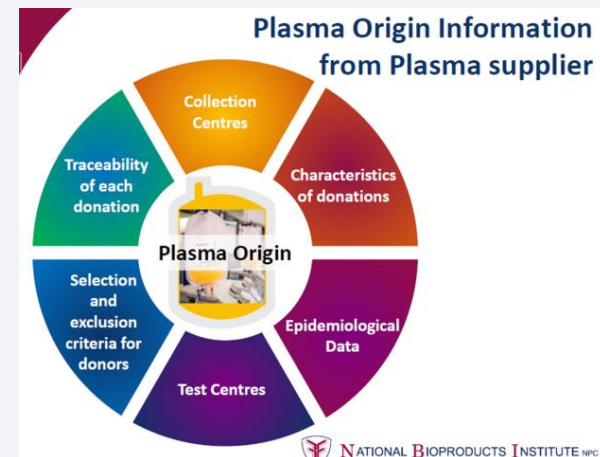
National/ Regional program with fractionators, a win-win situation

➤ For the collector/country client

- ✓ Improvement of quality level of blood & blood components and plasma collection by implementing same qualification procedure and systems programs in experienced BEs / countries;
- ✓ Grouping of collection centers; technical platforms for testing; plasma freezing,...
- ✓ Progress towards multiple products apheresis and plasmapheresis collection with the aim of best cost-effectiveness
- ✓ Increase of authorities' involvement
- ✓ Improvement in virus epidemiology surveillance data monitoring & Sensitization of the population to blood safety issue
- ✓ Ethical best use and avoidance of destruction of collected recovered plasma
- ✓ Stable supply of wide range of PDMPs for the patients in the country /region
- ✓ PDMPs Cost stability through long-term contracts avoiding flexibility of Ig prices
- ✓ Strategic independence in PDMPs
- ✓ If excess production of e.g., coagulation factors, optimisation of the donor's gift as humanitarian use towards neighbour countries

➤ For the fractionator

- ✓ Use of spare capacity of the plants (cost-effectiveness)
- ✓ Market entry in the country/region
- ✓ Supply of additional amounts of PDMPs manufactured from main production
- ✓ Closer relationship with competent authorities



Main Challenges for implementation

- Non engagement of Ministries of Health, Authorities

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“Absence of adequately resourced regulatory oversight, precluding assurance that appropriate standards are met at all stages of plasma production”

In 2018, 72 % of reporting countries, or 123 out of 171, had a national blood policy. Overall, 64% of reporting countries, or 110 out of 171, have specific legislation covering the safety and quality of blood transfusion, including:

- 79% of high-income countries
- 63% of middle-income countries
- 39% of low-income countries.

WHO Blood Safety and Availability Report June 2020

- Lack of financial resources or manpower/knowhow
- Volumes offered for fractionation // Lack of pathways for small volumes
- Non willingness of fractionators to invest in the quality learning process of several BEs
- Failure to meet internationally recognized quality and safety standards for recovered plasma
 - “Deficiencies in GMP compliance resulting in failure to utilize recovered plasma to make PDMPs constitute an unethical waste of valuable human resources”*
- Variability of the spare production capacity of the fractionator

Legal instruments



European
Commission



English

Home > Live, work, travel in the EU > Coronavirus response > Emergency Support Instrument

Emergency Support Instrument

Plasmapheresis equipment

On 11 January 2021, the Commission announced the [selected](#) 24 projects that will build new programmes, or expand existing ones, to collect plasma from donors recovered from COVID-19 and to build preparedness for the rapid collection in the event of future peaks or waves of the pandemic. The projects, which will take place in 14 Member States and the UK, are national or regional and will, in most cases, involve distribution of funds down to large numbers of local blood or plasma collection centres (over 150 in total).

Example

Ways to No Wastage from LMIC Country bilateral and regional cooperation to pooling EU collections

Upgrading Standards and Quality management in Blood Establishments, using

- sponsoring, funded training programs

“By combining plasma from countries whose national regulatory authorities have high maturity levels for blood regulation ..., the combined plasma may be offered to the fractionator...”

“Bringing the same Quality management program in all BE ... in contiguous coordinated countries to increase the volume of plasma and the burden on reaching right Quality level.”, increasing the chances of acceptance by the fractionator

Chapter 6. Country bilateral and regional cooperation

“Pooling of plasma from multiple countries within a region may be considered as a means to increase the cost-effectiveness of the fractionation, in agreement with the authorities of the countries and the fractionator”

=> Could be used for best usage of various small EU MS or Countries collections

⇒ Make it a regulatory tool

What can be done to redirect plasma for patients' needs?

- Make every attempt not to waste recovered plasma but make it quality available for fractionation
- Blood establishments take active role in collection of plasmapheresis plasma along with blood collection
Take into consideration societal aspects
A long-term and sustainable solution to safeguard this resource
- Authority's involvement // Blood and blood components governance in the EU Countries, MS
- Establish new Regulatory/Quality pathway = pooling of plasma from multiple small European Countries, MS

Whether the plasma is fractionated locally or elsewhere, there should be an ongoing dialogue between the collectors and the users (buyers) of PDMPs: plasma is needed for PDMPs locally or regionally to ensure patients' access to products while avoiding imbalance between plasma collection and access to treatment.

The End

Thank you for your attention

Back-up Slides

What is Contract Fractionation



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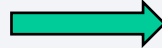
GLOSSARY

Contract plasma fractionation

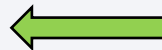
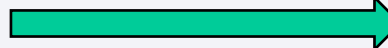
An arrangement in which domestic plasma is provided to a fractionator licensed in a foreign country and PDMPs are provided in return, according to predetermined terms for use within the country.

GLOSSARY ix

Local



Transport

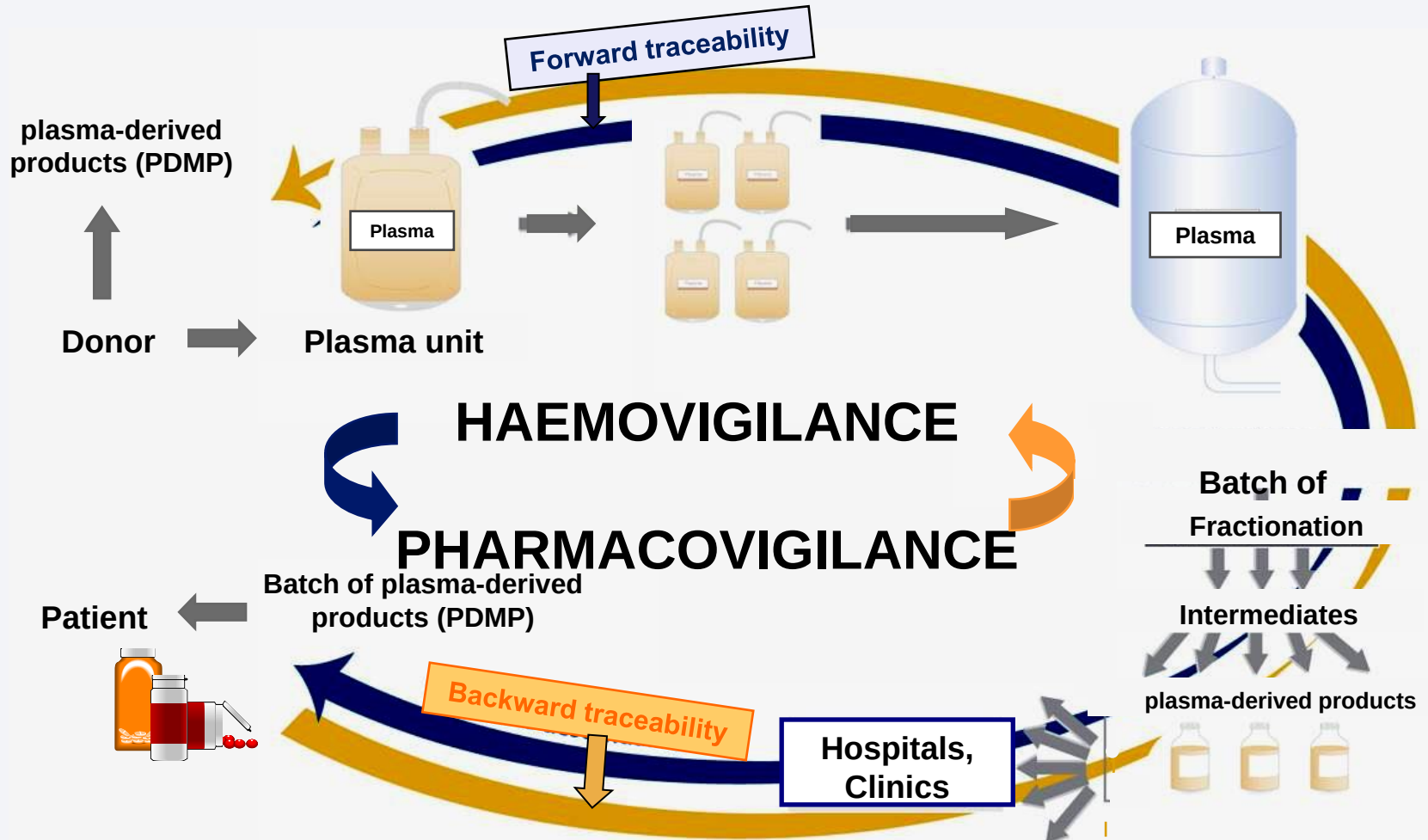


Abroad



Traceability of plasma units and blood monitoring system (look-back management) HV/PV

Additional Safety for recovered plasma, thanks to vigilance on recipients of labile products



Quality Contracts

Mandatory Quality Agreements

A regulatory requirement



Detailed « list of specifications », legally binding documents between the plasma supplier and the fractionator

Good communication between plasma suppliers and fractionators paramount, especially to anticipate and mitigate regulatory and quality constraints

Regulatory Constraints

If fractionation plant is located in EU,

✓ EU GMPs Annex 14 applies

With special chapters for contract fractionation programs (parts thereof apply)

Quality and Audit requirements of the Fractionator for the qualification of collection centers by fractionator => Benefits for the Blood Establishment

Written Agreements and Audits, a regulatory requirement for fractionator
an opportunity to Develop a culture of quality,

- Opportunities for improvements/ Address open issues in persons
- Confirmation of compliance level by an external party
 - Identification of items for improvement
 - Implementation of CAPA (Corrective Actions and Preventive actions)
- Building expertise within the BEs
- Definition of Roles and Responsibilities (BE - Fractionator)
- Anticipate impacts of regulatory changes
- **Readiness for Regulatory Competent Authority Regular Inspections**

