Introduction

- House keeping information
- EDQM / EU Commission, not to be confused
- Regulatory framework
<table>
<thead>
<tr>
<th>Council of Europe (SXB)</th>
<th>European Union (BRU)</th>
</tr>
</thead>
<tbody>
<tr>
<td>• 47 Member States</td>
<td>• 28 Member States</td>
</tr>
<tr>
<td>• 12 countries in 1949</td>
<td>• 6 countries in 1951,</td>
</tr>
<tr>
<td>• to promote democracy, human rights, rule of law</td>
<td>• European Coal and Steel Community, EEC, EU</td>
</tr>
<tr>
<td>• Conventions, CM res/rec</td>
<td>• Treaties (Rome 1957, Maastricht 1993, ...)</td>
</tr>
<tr>
<td>• European Pharmacopoeia in 1964 (38 MS &amp; EU)</td>
<td>• Single market, free movement: Goods, incl. Pharmaceuticals</td>
</tr>
<tr>
<td>• Public health by common quality standards</td>
<td>• Minimum safety and quality requirements: blood &amp; blood</td>
</tr>
<tr>
<td></td>
<td>components &amp; pharmaceuticals)</td>
</tr>
</tbody>
</table>
Democracy – Human Rights – Rule of Law

Council of Europe (SXB)
820 Million of Europeans

European Union (BRU)
500 Million of Europeans
From Donor to Patients, European Legislation

**Blood Legislation**
- Dir 2002/98/EC
- Dir 2005/62/EC
- Art. 2.2 GPG
- Dir 2016/1214/EU
- GPG CoE Guide

**Pharmaceutical Legislation**
- EU GMP Annex 14, rev 1
- Dir 2001/83/EC as amended
- European Pharmacopoeia

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Evaluation EU Legislation

Have the 2002 (blood) and 2004 (T&C) EU legislations increased safety and quality, and are they still up to date?

Knowledge gathered from:
- Implementation issues and reports
- Exchanges with National Authorities
- Stakeholder Forum
- Open Public Consultation
- Expert Study (literature, interviews, focus groups, …)
- Bilateral Meetings
- Multi-lateral Meetings EU-national-stakeholders. …

200+ submissions, incl all key stakeholder associations:
- **Overall, the Directives have improved safety and quality, which would have been hard to achieve without EU level.**
- **Legislation is not adaptable enough to manage risks (e.g., outbreaks, like ZIKA) and changes (e.g., technologies)**
- **Some key provisions are missing (like donor protection)**
- **Need for good coherence and interaction with medicinal framework (e.g., for plasma derivatives)**

Further collaboration EU – CoE (Grant)

1. commonly agreed standards in the field of T&C (+ dissemination)
2. biovigilance (SARE exercises) blood and T&C (data analysis and training)
3. Harmonising activity data collection exercises in T&C
4. Post-mortem blood testing practices for tissue donation
5. Testing performance of European BEs; Implementing QMS in BEs and EU requirements/CoE standards
6. Continuity of (1) blood supply,(2) plasma for fractionation and donor protection
Review of current practices reported in the survey conducted by the TS093 working party

Rut Norda, Uppsala University Hospital
Survey with 49 questions: data collection Sept-Dec 2017

- Apheresis for plasma for fractionation
- Compensation/reimbursement
- Collection practices
- Eligibility and medical assessment
- Blood tests
- Red cell loss
- Donor panel demographics
- Capture and recording of adverse reactions and events
- Qualification and supervision of staff
- Site requirements
- Productivity measures and key performance indicators
- Equipment used
Introductory remarks

• In this presentation:

• **The Guide** is the Council of Europe (CoE) Guide to the preparation, use and quality assurance of blood components

• **Standards** in the Guide can be Eu-directives, requirements from the Good Practice Guidelines or other Guide standards

• **BE** is the responding blood establishment (BE) that provided detailed information to the particular question in the survey
Responses: 36 BE in 25 countries

17 BE in 9 member states of CoE, and

7 BE in 7 other countries

• do collect plasma for fractionation by plasmapheresis and responded to the survey

Plasmapheresis collections last fiscal year (LFY):

• 2 888 390 donations (data provided by 22 BE)

• 652 379 donors (data provided by 16 BE)

Male donors: 61 % (min-max: 40 % – 97%) (data provided by 19 BE)
“Do your donors receive any form of compensation or remuneration (e.g., monetary payments for time and travel, a day off work, gifts of commercial value)? If so, please specify”

<table>
<thead>
<tr>
<th>Response</th>
<th>Number of Responders</th>
</tr>
</thead>
<tbody>
<tr>
<td>Compensation for time and travel</td>
<td>3</td>
</tr>
<tr>
<td>Fixed amount per donation</td>
<td>7</td>
</tr>
<tr>
<td>Token or Gift</td>
<td>3</td>
</tr>
<tr>
<td>Reward Program</td>
<td>1</td>
</tr>
<tr>
<td>None</td>
<td>10</td>
</tr>
</tbody>
</table>
Guide standards for plasmapheresis per donor and year
- max 750 mL, excl. anti-coagulants, per donation
- max 33 plasmapheresis donations
- max 25 L plasma

<table>
<thead>
<tr>
<th>Practices compared to Guide standards</th>
<th>BE: lower/aligned</th>
<th>BE: higher</th>
</tr>
</thead>
<tbody>
<tr>
<td>Collection volume</td>
<td>15</td>
<td>9</td>
</tr>
<tr>
<td>Donations</td>
<td>15</td>
<td>8</td>
</tr>
<tr>
<td>annual volume</td>
<td>17</td>
<td>7</td>
</tr>
</tbody>
</table>
### Practice versus standards: donations per donor LFY

CoE Guide standard: max 33 donations per year

<table>
<thead>
<tr>
<th>Number of donations per donor and per 12-month period</th>
<th>1-5</th>
<th>6-10</th>
<th>11-15</th>
<th>16-20</th>
<th>21-25</th>
<th>&gt; 25</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aligned/lower than Guide 11 BE: 611 833 donors and 2 062 034 donations</td>
<td>82%</td>
<td>16%</td>
<td>4%</td>
<td>1%</td>
<td>1%</td>
<td>0%</td>
</tr>
<tr>
<td>Higher than Guide 5 BE: 40 456 donors and 561 622 donations</td>
<td>39%</td>
<td>15%</td>
<td>11%</td>
<td>7%</td>
<td>7%</td>
<td>21%</td>
</tr>
</tbody>
</table>

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Methods to decide collection volume

Guide standard: total blood volume must be estimated

<table>
<thead>
<tr>
<th>Method</th>
<th>BE</th>
<th>Collections</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bodyweight (with max volume)</td>
<td>11</td>
<td>783,306</td>
</tr>
<tr>
<td>(data by 10 BE)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gender, weight and height</td>
<td>6</td>
<td>1,306,789</td>
</tr>
<tr>
<td>Algorithm in equipment</td>
<td>2</td>
<td>42,557</td>
</tr>
<tr>
<td>Standard volume</td>
<td>2</td>
<td>15,298</td>
</tr>
<tr>
<td>XXX protocol</td>
<td>1</td>
<td>703,857</td>
</tr>
<tr>
<td>Not specified</td>
<td>2</td>
<td>36,533</td>
</tr>
</tbody>
</table>
# Medical assessment

<table>
<thead>
<tr>
<th></th>
<th>At first donation</th>
<th>At repeat donations</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Everytime</td>
</tr>
<tr>
<td>DHQ+interview</td>
<td>23</td>
<td>18</td>
</tr>
<tr>
<td>Weight</td>
<td>19</td>
<td>16</td>
</tr>
<tr>
<td>Height</td>
<td>5</td>
<td>2</td>
</tr>
<tr>
<td>Hb</td>
<td>22</td>
<td>18</td>
</tr>
<tr>
<td>Blood pressure/ pulse rate</td>
<td>21/19</td>
<td>17</td>
</tr>
<tr>
<td>Body temperature</td>
<td>7</td>
<td>7</td>
</tr>
<tr>
<td>Physical exam</td>
<td>8</td>
<td>1</td>
</tr>
</tbody>
</table>

*13 require a higher level of Hb than Guide standard for plasmapheresis*
# Screening for infectious markers

<table>
<thead>
<tr>
<th>21 BE</th>
<th>At first donation</th>
<th>At repeat donations</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Standard</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HIV and HCV serology</td>
<td>20</td>
<td>20</td>
</tr>
<tr>
<td>HBsag</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HIV/ HBV/ HCV NAT</td>
<td>16/14/15</td>
<td>16/14/15</td>
</tr>
<tr>
<td>Syphilis ab</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>Other tests</td>
<td>7</td>
<td>7</td>
</tr>
</tbody>
</table>
Standards: total protein, electrophoresis (SPE) or albumin and IgG before start and at least annually. ABO RhD may be waived

<table>
<thead>
<tr>
<th>22 BE</th>
<th>At first donation</th>
<th>At repeat donations</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Every time</td>
<td>Other frequency, at least annually</td>
</tr>
<tr>
<td>IgG, some incl. IgA and/or IgM</td>
<td>20</td>
<td>2</td>
</tr>
<tr>
<td>Total protein</td>
<td>17</td>
<td>5</td>
</tr>
<tr>
<td>Albumin</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Full blood count</td>
<td>15</td>
<td>9</td>
</tr>
<tr>
<td>ABO/RhD</td>
<td>19</td>
<td>12</td>
</tr>
<tr>
<td>RBC ab screening</td>
<td>20</td>
<td>7</td>
</tr>
</tbody>
</table>
# Practices to capture and report donor adverse events

Guide standard: report all adverse events

<table>
<thead>
<tr>
<th>Adverse events captured</th>
<th>All</th>
<th>Selected</th>
</tr>
</thead>
<tbody>
<tr>
<td>BE</td>
<td>20</td>
<td>4</td>
</tr>
<tr>
<td>Reporting system used</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Electronic system</td>
<td>16</td>
<td>2</td>
</tr>
<tr>
<td>Other system</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Not specified</td>
<td>1</td>
<td></td>
</tr>
</tbody>
</table>
### Adverse event surveyed rate/10 000 collections requested

<table>
<thead>
<tr>
<th>Type of adverse event</th>
<th>Respondents</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall adverse event rate</td>
<td>18</td>
</tr>
<tr>
<td>Acute vasovagal reaction, no loss of consciousness</td>
<td>18</td>
</tr>
<tr>
<td>Acute vasovagal reaction, loss of consciousness</td>
<td>17</td>
</tr>
<tr>
<td>Delayed vasovagal reaction, no loss of consciousness</td>
<td>17</td>
</tr>
<tr>
<td>Delayed vasovagal reaction, loss of consciousness</td>
<td>16</td>
</tr>
<tr>
<td>Citrate reaction</td>
<td>16</td>
</tr>
<tr>
<td>Haemolysis</td>
<td>19</td>
</tr>
<tr>
<td>Extravasation</td>
<td>12</td>
</tr>
</tbody>
</table>

Varying number of respondents negated various types of events

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Apheresis equipment used LFY

<table>
<thead>
<tr>
<th>Equipment</th>
<th>BE</th>
<th>Collections</th>
</tr>
</thead>
<tbody>
<tr>
<td>PCS2, MCS+, ns</td>
<td>13</td>
<td>750 258</td>
</tr>
<tr>
<td>Mixed</td>
<td>5</td>
<td>927 174</td>
</tr>
<tr>
<td>Trima</td>
<td>1</td>
<td>573 624</td>
</tr>
<tr>
<td>Aurora</td>
<td>1</td>
<td>6 328</td>
</tr>
<tr>
<td>Not indicated</td>
<td>3</td>
<td>643 756</td>
</tr>
</tbody>
</table>

Mixed: equipment from at least two different manufacturers
Summary and conclusions

- Most donors donate less often and less volume than recommended by Guide standards
- Medical assessment of donors is always or almost always performed according to Guide standards
- Product safety is always or almost always supervised according to Guide standards
- Capture and recording of ARE should be harmonised
Voice of the patients:

patient perspectives & views
situation & future needs in PDMPs

Frank Willersinn, MD
alpha1plus@yahoo.be
Conflicts of interest
> none

patient representatives &

IPFA
EBA
EPA
PPTA
IFBDO
...

Int.Symp. 'Plasma Supply Management',
Strasbourg, Jan. 28/29th 2019
Some views from the patient perspective

1. About the patient

2. Some diseases treated by PDMP
   * AATD
   * Hemophilia & RBD
   * PID
   * GBS – CIPD – MMN
   * C1 E I

3. Obstacles to strategic independence of plasma

4. Proposals to increase availability

5. Conclusion / last ideas
About the patient

- Life threatening medication

- Avoiding crisis or situations of emergency

- Quality of life & social welfare
  - pain
  - security
  - social life & integration
  - well being

THE PATIENT DOES NOT CARE WHERE HIS PRODUCT COMES FROM – BUT HE IS GRATEFUL!
disease: Alpha-1 antitrypsin deficiency

Genetic
Rare disease
Liver (newborns) & lung (emphysema COPD)
oxygen
Lung transplant
Name of the patient: Frank

* 1953
  1996
  1998
  2008

2019 FEV > 60%

lungtransplant
THE PATIENT DOES NOT ASK WHERE HIS PRODUCT COMES FROM –

BUT HE IS GRATEFUL
2. Some treatments by PDMPs

Alpha-1 antitrypsin deficiency

47/15
ZZ 12.000/120.000
Underdiagnosed +++
Shortages / not deliverable

treatment for 1 year: 900 donations
Hemophilia and Rare Blood Diseases

Europe 100.000
Not really underdiagnosed
+-
Incidence of Haemophilia and RBDs: ~100,000

- Haemophilia A (VIII) 1:10,000
- Haemophilia B (IX) 1:50,000
- VWD 1:50,000 (1:100)
- Factor I 1:1 million
- Factor II 1:2 million
- Factor V 1:1 million
- Factor VII 1:500,000
- Factor X 1:1 million
- Factor XI (C) 1:100,000
- Factor XIII 1:3 million

Brian O’Mahony 2014
Primary immunodeficiency

20 000 Registry / 370 000 estimated in Europe
Underdiagnosed
+++ 
Shortages 2017/2018 Romania, UK, Cyprus, France,...
++

Plasma donation 5-15g >> 100 donations for 1 year
PID patient: for 75 years: 100 000 donations

Once a medication is integrated in a NHS shortages are unacceptable
GPS - Guillain-Barré syndrome
CIDP - Chron. Inflamm. Demyelinating Polyneuropathy
MMN - Multifocal Motor Neuropathy

~3000 / Europe
Incidence / prevalence

- GBS Incidence: 0.62 - 2.66 / 100,000
- CIDP Prevalence: 1-8 /100,000
- MMN: prevalence 1 / 100,000
Treatment for GBS, CIDP and MMN: IV Ig

**GBS:** 0.4 g/kg for 5 days

**CIDP:** loading dose 2 g/kg, 2–5 days
then 1 g/kg every 3 weeks for 6 months or longer

**MMN:** 2 g/kg 2–5 days
maintenance 1 g/kg every 2–4 weeks

INCBASE & PREDICT study:
improvement of diagnosis >> increasement of IgG
C-1 esterase inhibitor

Prevalence Italy: 1/65000
Not really underdiagnosed +/-
Some shortages (F, UK, D...)

next 5 years: number of patients will not grow much
## Future needs

<table>
<thead>
<tr>
<th></th>
<th>AATD</th>
<th>Hemo + RBD</th>
<th>PID</th>
<th>GPS</th>
<th>C1 IE</th>
<th>Alb</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>More indications</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Shortcuts</strong></td>
<td>+</td>
<td>+</td>
<td>?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Underdiagnosed</strong></td>
<td></td>
<td>VW factor</td>
<td></td>
<td></td>
<td>+/-</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Needs next 5 years</strong></td>
<td>++</td>
<td>+/-</td>
<td>+++</td>
<td>+</td>
<td>same</td>
<td>+</td>
</tr>
</tbody>
</table>
3. Some obstacles to strategic independence of plasma

47 countries - more than 40 Public Health Care Systems
EUROPE: more than 250 languages

HTA is heterogenious event:
- Based on cost / effectiveness, less on clinical efficacy
- HTA models poorly accepted in R.D.

Economical crisis: 10 years / 69 years

less flexibility of management or synergy >> shortages

Orphan drug regulation (exclusivity...)

European independance soon >> but Global self-sufficiency is the goal
4. proposals to increase availability

740 million people: plasma donation is ‘not known’ ?

>> Make it known !

Métro advertising, Brussels, July 2018
to create awareness: an issue of communication

Explain → convincing → motivation

sensitization

donation
**Education:**

Health is a major issue in well-being

<table>
<thead>
<tr>
<th>Sensitize</th>
<th>in universities, schools (get nurses to schools as health educators)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Create awareness</td>
<td>about Rare Diseases</td>
</tr>
<tr>
<td></td>
<td>about the need for plasma &amp; possibilities to donate</td>
</tr>
<tr>
<td>Create tools to communicate</td>
<td>to patients in an understandable language</td>
</tr>
<tr>
<td></td>
<td>to the medical community in an easy way</td>
</tr>
</tbody>
</table>
International Blood & Plasma Day: June 14th
Create new values:

Donation can be a social value of identity & recognition
Create new values:

Altruisme

can be a social value of integrity
and source of quality of life
« 2025 »
multipliscinary crew / transversal think tank

- Psychologist
- Sociologist
- Zukunftsinstitut
- young mother
- plasma insider
- ... 

« which ‘ideas’ will make people make donate in 2025 ? »
...when marketing meets communication:
Netherlands 2019: donor recruitment for rare blood groups
Also:

- Promote plasmapheresis programs where feasible
- Plasma from hemochromatosis patients
- Honor the donor: new definition of Compensation
- Get better National plasma donor database
Management for supply and availability:
Flexibility of firms, of countries

Standards of Quality
Also: quality of charges,
efficacy of molecules,
>> personalized medicine

Pharmacovigilance:
Data collection of side effects,
patient reported outcomes
Who is motivated today?

Renate

- friend
- aunt
- colleague
- neighbour

PLUS Stakeholder meeting, Brussels
September 17th 2018
Cooperation

Interaction

Compromises

lexibility

synergy

Work out more altruisme

Educate!

The patient needs you!

Int.Symp. 'Plasma Supply Management', Strasbourg, Jan. 28/29th 2019
PLUS Consensus Principles on Strategies
to encourage Blood and Plasma Donations in Europe

The Platform of Plasma Protein Users organised a Consensus Conference in Estoril, Portugal on 24-25 January 2019 bringing together different stakeholder organisations active in the field of blood and plasma collection and fractionation.

The following key principles were identified and endorsed by the stakeholders listed below during the meeting. This is done with a view to inform future policy discussions in Europe around the collection of blood and plasma.

These principles will also be helpful in the context of a potential revision of the EU Blood Directive.

1. Recognition that Plasma Derived Medicinal Products (PDMPs) are life-saving therapies.
2. Patient organisations representing the communities dependent on a stable supply of PDMPs should be involved in policy decision-making.
3. Patient organisations call for global sufficiency of PDMPs as the ultimate goal of any regional effort to collect more plasma.
4. Any measure or new policy aimed at increasing blood and plasma collection should ensure that it is both patient- and donor-centred, with the goal to meet growing clinical needs.
5. Education on health questions regarding blood and plasma should be promoted throughout Europe.
6. All measures and policies should respect and promote health and safety for patients.
7. All measures and policies should respect and promote quality, safety of blood and plasma collection, including donors' safety.
8. In the interest of transparency, blood and plasma donors should be informed about how their donation can be used.
9. Measures to increase blood collection may be different from the ones aimed at increasing plasma collection.
10. Plasma collection through plasmapheresis is key to ensure Europe can increase its supply of plasma for fractionation.
11. Avoiding wastage of recovered plasma is also important.
12. All manufacturers should be encouraged to use recovered and/or apheresis plasma.
13. Future European policies should take into consideration the differences between blood and plasma collection as well as between labile blood products and plasma derived medicinal products (PDMPs).
14. In doing so, European policies should acknowledge the possibility of co-existence of both the public and private sector involved in blood and plasma collection.

15. Good Manufacturing Practices / Good Practices and testing requirements of the European Medicines Agency Plasma Master File should be implemented.

16. Clarification of terminologies / definitions in European legislation is required to support better coordination of blood and plasma collection.

Estaril, January 23rd 2019

Stakeholders endorsing:
- Alan Weil (World Federation of Hemophilia)
- Albert Farrugia (University of Western Australia)
- Bob Perry (International Plasma and Fractionation Association)
- Dominika Mierzwa (Plasma Protein Therapeutics Association)
- Frank Willemsen (Platform of Plasma Protein Users, Alpha 1 Global)
- Jan Rut (Plasma Protein Therapeutics Association)
- Johan Prevost (Platform of Plasma Protein Users, International Patient Organisation for Primary Immunodeficiency)
- Joss Oudin (International Patient Organisation for Primary Immunodeficiency)
- Karl Petrovsky (Plasma Protein Therapeutics Association)
- Édité Soos (International Patient Organisation for Primary Immunodeficiency)
- Frans Kroeker (World Federation of Hemophilia)
- Mark Sieben (American Plasma Users Coalition)
- Martin van Hagen (Rotterdam Erasmus Medical University Hospital, International Patient Organisation for Primary Immunodeficiency)
- Martine Bergère (International Patient Organisation for Primary Immunodeficiency, IRIS)
- Patrick Bérouard (Guillain-Barré Syndrome/Chronic Inflammatory Demyelinating Polyneuropathy, Multifocal Motor Neuropathy)
- Patrick Roberts (Market Research Bureau)
- Paul Strengers (International Plasma and Fractionation Association)
- Sara Kiefer (International Patient Organisation for Primary Immunodeficiency)
- Stephan Wallemann (European Plasma Alliance)

Ed. resp. Johan Prevost, PLUS. Av. Aida, Bloco 8, Esc. 321, 2705-187 Estaril, Portugal. johan@plus.pt
Is yearly collection of recovered / apheresis plasma adequate to ensure European self-sufficiency of essential plasma derived medicinal products?

Paul Strengers

Symposium jointly organised by the EDQM and the EU Commission
29-30 January 2019
Strasbourg, France
Questions regarding the title

• Yearly collection
• Recovered / apheresis plasma
• European self-sufficiency of PDMPs

OR

• European self-sufficiency of plasma
of 27 January 2003
setting standards of quality and safety for the collection, testing, processing, storage and distribu-
tion of human blood and blood components and amending Directive 2001/83/EC

In adopting Directive 89/381/EEC, which covers blood and plasma as the starting material for the preparation of medicinal products, Council accepted Community self-sufficiency (as distinct from national self-sufficiency) through voluntary unpaid blood and plasma donations as a goal. Its attainment, however, is influenced by several factors: the willingness of the citizens of the Member States to donate blood and plasma; the interpretation in the Member States of non-remunerated donations as defined by the Council of Europe; optimal use of these products by treating physicians taking fully into account the very special nature of their source; and differing regulations and practices in the Community which may restrict the exchange of blood and blood products between Member States and hinder the attainment of self-sufficiency.
This presentation

• European self-sufficiency of PDMPs
• Adequate collection of recovered / apheresis plasma
European self-sufficiency of PDMPs
The position of PDMPs in the health care landscape

- Indicated for rare diseases
- More and more indications identified
- Increasing number of patients in Europe and worldwide
- Expected increasing demand from developing countries
- Limited alternative treatments available
- High and increasing pricing
- Price differs per continent and per country
- Pressure on health care costs in general
- Questions on position of and margins for industry
Definition of self-sufficiency mostly often referred to

Self-sufficiency in safe blood and blood products based on VNRBD means that the national needs of patients for safe blood and blood products, as assessed within the framework of the national health system, are met in a timely manner, that patients have equitable access to transfusion services and blood products and that these products are obtained from VNRBD of national, and where needed, of regional origin, such as from neighboring countries.

Challenges on self-sufficiency of PDMPs:

• Not a proper definition
• The demand for the most wanted PDMP (currently IgG) is the trigger for the volume of plasma needed

• Which level of self-sufficiency is needed: 50 - 80% or even 100%?
• Does self-sufficiency based on EU plasma imply exclusion of products manufactured from non-EU plasma?
• If the demand for PDMPs grows, can the supply of plasma follow (or even better: has the volume been collected in advance)?
Global IgG demand – Actual and Projected

What is to be expected when Asia and Africa with their dense and increasing population become integral part of the global market?
IVIG & SCIG CONSUMPTION BY COUNTRY IN EUROPE
2008 – 2025 - Kilograms

Total Europe 2025: 67,368 Kg.
Current situation on provision of PDMPs in Europe

2017-2018 United Kingdom:
IVIG. Insufficient supply, supply instability, reduction of products commissioned, cost containment, cheapest products only, company withdrawal from market.

2018 France:
IVIG. Supply tensions.

2018 Netherlands:
Hyper immune IgG. Supply tensions.

2018 Romania:
IVIG. Supply withdrawal from market due to clawback tax set by government

Other countries with supply tensions: Cyprus, Germany, Greece, Hungary, Latvia, Lithuania, Portugal.
Increasing pricing of IVIG

Figure 3.5: Global IG Market (Average Sales Price Per Gram)

Aim: not self-sufficiency, but strategic independence

Strategic independence has the objective to create a balance against the current dependency from the source plasma supply from the US.

Geographic imbalance in plasma collection concerns that local disruptions of plasma supplies could result in regional and global shortages of PDMP’s:

- emergence unexpected transfusion-transmissible infections [remember vCJD]
- commercial consolidation
- changes in demand
- flow of medicines from low price to high price countries [Romania IgG crisis]

Ref.: Transfusion 2016; 56:3133–3137
Adequate collection of recovered / apheresis plasma
### PLASMA VOLUME REQUIREMENTS TO MEET THE DEMAND FOR POLYVALENT IMMUNOGLOBULIN CONSUMPTION IN EUROPE - 2008-2017 (Kilograms, Liters)

<table>
<thead>
<tr>
<th></th>
<th>2017</th>
<th>Shortfall of Plasma for fractionation (Liters)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>IgG Consumption (Kilograms) (a)</td>
<td>Volume of Plasma Liters 4 grams/liter Needed - yield (b)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Recovered (Liters) (c)</td>
</tr>
<tr>
<td>France</td>
<td>10,873</td>
<td>2,718</td>
</tr>
<tr>
<td>Germany</td>
<td>9,032</td>
<td>2,258</td>
</tr>
<tr>
<td>Italy</td>
<td>5,500</td>
<td>1,375</td>
</tr>
<tr>
<td>Spain</td>
<td>4,203</td>
<td>1,051</td>
</tr>
<tr>
<td>United Kingdom</td>
<td>5,821</td>
<td>1,455</td>
</tr>
<tr>
<td>Rest of Europe</td>
<td>15,041</td>
<td>3,760</td>
</tr>
<tr>
<td>Total Europe</td>
<td>50,470</td>
<td>12,618</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>2025</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>IgG Consumption (Kilograms) (a)</td>
<td>Volume of Plasma Liters 4 grams/liter Needed - yield (b)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Recovered (Liters) (c)</td>
</tr>
<tr>
<td>France</td>
<td>15,453</td>
<td>3,863</td>
</tr>
<tr>
<td>Germany</td>
<td>12,033</td>
<td>3,008</td>
</tr>
<tr>
<td>Italy</td>
<td>6,007</td>
<td>1,502</td>
</tr>
<tr>
<td>Spain</td>
<td>5,428</td>
<td>1,357</td>
</tr>
<tr>
<td>United Kingdom</td>
<td>7,445</td>
<td>1,861</td>
</tr>
<tr>
<td>Rest of Europe</td>
<td>21,086</td>
<td>5,272</td>
</tr>
<tr>
<td>Total Europe</td>
<td>67,453</td>
<td>16,863</td>
</tr>
</tbody>
</table>

Additional plasma volume required between 2017 and 2025 (liters x 000) 3,880
Assume 9% annual growth of source plasma collections between 2017 and 2025
The Growing Discrepancy between the Domestic Supply of Plasma and the Needs to meet IgG Demand from 2011 to 2025

The Domestic Plasma Procurement does not catch up with the growing need for plasma to make IgG in Europe

Ref. P. Robert, PLUS conference 2019, 24-01-2019
The Growing Discrepancy between Recovered and Source Plasma in the Domestic Supply from 2011 and 2025

The share of source plasma increases while recovered plasma's declines

Ref. P. Robert, PLUS conference 2019, 24-01-2019
Number of registered blood donors in European countries

Ref.: European Blood Alliance report, 2015
Plasma donation and willingness

Ref.: Merz, Eurobarometer, unpublished data
Plasma donors, motivations and intentions

Method:
- Study on N=4,861 new donors
- Questionnaire on motivations and intentions (response rate 61%)

Results:
- Plasma donors had higher intentions, self-efficacy, positive attitudes, lower anxiety compared to whole blood donors
- Higher intention → higher odds to become plasma donor

Conclusions:
- Motivational differences exist before very first donation
- Self-efficacy and confidence especially salient for plasma donors

Ref.: Veldhuizen & Van Dongen 2013, Transfusion
Challenges on availability of PDMPs

- Medicines are only meaningful, if we can afford them
- For the treatment of rare diseases, a free market has its limitations
- Transfer of product to highest priced market is harming
Challenges on European self-sufficiency of PDMPs based on EU plasma

- European recovered plasma and apheresis plasma should be made available more for manufacturing
- More European plasma for manufacturing alone is not enough
- Companies will use this plasma for manufacturing of PDMPs
- Only on well thought-out contracts, these PDMPs will be made available for European patients
- Otherwise, companies will aim for markets with the highest margin
- IPFA members have national mandate and will prioritize their home markets
Summary for EU and Council of Europe

- The willingness of European citizens to donate plasma is present
- Plasma be a strategic resource should be the aim
- As should be strategic independence of plasma and PDMPs in Europe
- Promote and support awareness programmes for rare diseases
- Promote and support awareness programmes for plasma donation
- Blood and plasma donors should be informed about how their donation can be used
- Social justice, a quality in Europe, should be maintained
Thank you for your attention
“THE KEY IMPORTANCE OF DONORS AND THEIR ORGANISATIONS”
The IFBDO (or FIODS, in French) is the International Federation of Blood Donors Organizations, the network of national donors’ associations working for the promotion of voluntary, anonymous, regular, non remunerated blood and plasma donation.

The Federation was founded in 1955 and nowadays includes more than 80 members in 4 continents, representing more than 18 million of blood donors in the world.

It is organized in an Executive Council and Continental Committees, plus a Medical Counsellors Group and the International Youth Committee (IYC), the group of IFBDO member state volunteers between 18 and 30 years old.
FOOD FOR THOUGHT

I. The values of donation

II. Some critical issues

III. The occasion of the review of the EU Directives on blood, tissues and cells (proposals)
THE VALUES OF DONATION
Voluntary, anonymous, non-remunerated, regular donors are the "safest" allies for themselves and especially for the patients.

Donated blood (and plasma) should be seen as a public, ethical, strategical and community good in order to assure the dignity of the donor and of their donation and not as a commodity to meet others’ ends.

Donation is an act of solidarity for the benefit of others and contributes to social cohesion and civic engagement.

Blood donation is indeed a matter of health and human rights: donor rights and patient rights (Charter of Fundamental Rights of the EU, art. 3; Oviedo Convention on Human Rights and Biomedicine, art. 21).
The Donor Community

Associations are – in many cases – responsible for donor recruitment and donor retention (regular donors).

Associations play a strategic role not only for these major tasks, but also in raising awareness about the importance of voluntary non-remunerated donors in public health systems and in promoting the culture of solidarity, prevention and healthy lifestyles (in a complementary way to the actions of health authorities).

European Parliament resolution of 27 October 2016 on European Voluntary Service and the promotion of volunteering in Europe.
SOME CRITICAL ISSUES
FROM THE POINT OF VIEW OF DONORS

Blood donors are **generally available** to consider plasma donation.

However, sometimes plasma donation is – wrongly – perceived as a «second class» donation: it’s a matter of **culture** and delivering the right message.

Moreover, there are **concerns** about plasma donation: duration, fear of apheresis procedure.
Directive 2002/98/EC (art. 20) *encourages* Member States to collect 100% of donations of blood and plasma from voluntary and unpaid donors, but does not include any obligation (room for various interpretations).

Europe is not self-sufficient in PDMPs and imports the vast majority of the plasma required for the manufacture of medicines – dependence on just one country.

Beware the distinctions between blood and plasma donation.
DONOR COMMUNITY

**Speak clearly:** if well informed, blood donors (or new donors) would be prepared to donate plasma.

**Make it easy:** improve the efficiency of plasma collection, e.g. optimize blood banks opening hours.

**Donor care:** health protection; feedback and recognition to meet expectations; let donors understand the ethical importance of their gift as an expression of community participation in the health system.
WORKING TOWARDS SELF-SUFFICIENCY

Recognition, by the EU legislation, of blood products supply as a life-saving service of general interest.

Clear definitions (VNRD and self-sufficiency criteria).

Enlarge donor base.

Empowerment of organizations: where donor associations are present, the coverage of needs tends towards self-sufficiency.

Traceability, PDMP labeling.

Coordinated approach and common projects/plans to reach self-sufficiency for blood and blood components and PDMPs from VNRD across Europe.
Thank you!

Alice Simonetti
IFBDO/FIODS
a.simonetti@avis.it
Meeting the demand for plasma in The Netherlands

Plasma donor marketing revised

Mrs. D.C. Thijssen-Timmer

Member Executive Board - Director Blood Bank

Sanquin
Increasing dependency on US plasma

Plasma Collection Growth

EU + 2.9% CAGR

US + 9.8% CAGR

Source: Company information, equity research, Grifols analyst presentations
Need for more plasma donors who donate more frequently

Guiding principles:

- donor safety
- voluntary non remunerated

1000 Kg

Global IG Demand - Actual and projected

Source: Company information, equity research, Grifols analyst presentations
Donor recruitment channels

Registration new donors @Sanquin (2018)

- Spontaneous
- Donor recruits a donor
- Social media
- Corporate recruitment
- Collection site
- News letter matchis (stem cell recruitment agency)
- Media (other)
- Students
- Other

Male
Female

Percentage:
0%  5%  10%  15%  20%  25%  30%  35%  40%
Converting B+ and AB+ whole blood donors in plasmapheresis donors

A+
B+
AB+
O+
A−
B−
AB−
O−
Plasma donor recruitment

@ Sanquin

# first time plasma donors
Obstacles for plasma donor recruitment

Converting whole blood donors in plasma donors is not sustainable:

• Whole blood supply “at risk”
• Different proposition

Need for another proposition for plasmapheresis donors:

Whole blood donors: 3-5 times per year 15 minutes
Plasmapheresis donors: > 10 times per year 50 minutes
General results:

Donating blood/plasma feels more personal than donating money to charity.

Donating is considered to be done voluntary, although ‘medical check’ is considered a bonus.

Ex-donors mainly quit because of life events (child birth, divorce), but are willing to restart.

Motives of donors & non-donors

30 IN-DEPTH INTERVIEWS

Qualitative research

Market research Dec 2017, Sanquin & True Research, unpublished data
**Qualitative research**

Motives of donors & non-donors

30 IN-DEPTH INTERVIEWS

**General results:**

- Blood donors need more information to be converted in plasma donors.
- A mere minority of blood donors knows that hospitals pay for blood.
- Plasma donors know that hospitals pay for PDMP’s.

Market research Dec 2017, Sanquin & True Research, unpublished data.
Qualitative research

Motives of donors & non-donors

30 IN-DEPTH INTERVIEWS

It is unclear to donors why plasma donors are asked to come in more frequently

Key information:

Market research Dec 2017, Sanquin & True Research, unpublished data
Key information:

Donating more than 10 times per year feels like an obligation, which interferes with the feeling of ‘voluntary’ donation.

Market research Dec 2017, Sanquin & True Research, unpublished data
Qualitative research

Motives of donors & non-donors

30 IN-DEPTH INTERVIEWS

Donating for a good cause interferes with the ‘commercial interest’ of producing medicines

Key information:

Market research Dec 2017, Sanquin & True Research, unpublished data
"When I think about manufacturing pharmaceuticals, I do think of big money making machines."

(F, 36, ex-donor, Amsterdam)

More plasma donors would like a form of compensation when asked to donate more often.

Key information:

Market research Dec 2017, Sanquin & True Research, unpublished data
InPlace

a pilot center for cost efficient plasma collection

- Donor marketing
- Process optimalisation
- Optimal collection site
Pilot propositions for a sustainable plasma donor pool

• ‘Story telling’ (Donor story, Product Story, Patient Story)

• What incentives have best impact on frequency, loyalty, willingness?

• What does the donor want?
The principle of the prohibition of financial gain
(Committee on Bioethics (DH-BIO))

An intervention Ladder for promoting donation

1. INFORMATION about the need for the donation of bodily material for others' treatment or for medical research.
2. RECOGNITION of, and gratitude for, altruistic donation, through whatever methods are appropriate both to the form of donation and the donor.
3. INTERVENTIONS TO REMOVE BARRIERS AND DISINCENTIVES TO DONATION experienced by those disposed to donate.
4. INTERVENTIONS AS AN EXTRA PROMPT OR ENCOURAGEMENT for those already disposed to donate for altruistic reasons.
5. INTERVENTIONS OFFERING ASSOCIATED BENEFITS IN KIND to encourage those who would not otherwise have contemplated donating to consider doing so.
6. FINANCIAL INCENTIVES that leave the donor in a better financial position as a result of donating doing so.

Source: Human bodies: donation for medicine and research, Nuffield Council on Bioethics
Plasma donors in The Netherlands

Method:
• Use of Dutch consumer data (WHOZZ)
• Different segments based on wealth and age
• Defining current plasma donor population
• Defining target population plasma donors
Results
plasma donors in The Netherlands

Nov 2018; Sanquin & WHOOZ (Whize); unpublished data

Highly represented within current population
Age 30-55; mid-high educated
Age 55+; average income
Students

wealth

age
Results
plasma donors in The Netherlands

Nov 2018; Sanquin & WHOOZ (Whize); unpublished data

Donation frequency

Age 40-70: high frequency (> 8 times per year)

Students: low frequency (1-3 times per year)

wealth

age

9.0%
1.9%

9.2%
4.7%

12.2%
8.3%

8.9%
7.5%

5.7%
4.0%

8.8%
4.3%

9.9%
Target population

**Working, 40+**
- kids: none/ 12+
- middle education
- current donor profile of loyal/ high frequency donors

**(Pre-) Retirement, <70**
- current donor profile of loyal/ high frequency donors
- flexibility (daytime)

**Students**
- new donor profile
- ‘tomorrow’s donor’
- easy reachable (social media/ network)
- flexibility
- healthy
- large willingness to donate*

* Presentation: “Who gives life? Changes in (blood) donor behavior across different age groups” by Eva-Maria Merz, Sanquin Research – Donor studies
<table>
<thead>
<tr>
<th>What</th>
<th>When</th>
</tr>
</thead>
<tbody>
<tr>
<td>Define geographic location</td>
<td>Jan 2018</td>
</tr>
<tr>
<td>Impact analysis on whole blood donors (surroundings of defined location)</td>
<td>Feb 2018</td>
</tr>
<tr>
<td>Plasma Donors Journey</td>
<td>Feb-Mar 2018-2019</td>
</tr>
<tr>
<td>Proposals for recruitment strategy</td>
<td>Mar-Apr 2019</td>
</tr>
<tr>
<td>Procurement of machines, test, beds, etc.</td>
<td>Mar-May 2019</td>
</tr>
<tr>
<td>Start donor recruitment</td>
<td>May 2019</td>
</tr>
<tr>
<td>Official opening of center</td>
<td>Sep 1st 2019</td>
</tr>
<tr>
<td>Evaluation of first results</td>
<td>Jan-Mar 2020</td>
</tr>
</tbody>
</table>
Sanquin develops new strategies to increase plasma collection:

- New incentives, other forms of reimbursement, and possibly compensation
- In compliance with Oviedo convention & DH-BIO (no financial gain principle)
- In close cooperation with our European partners & Canada

Take home message

- Converting whole blood donors in plasma donors not sustainable to meet the growing demand for plasma
- Plasma donor wants a different proposition
LEARNINGS FROM THE FRENCH ATTEMPT TO CONVERT WHOLE BLOOD DONORS IN PLASMAPHERESIS DONORS

Dr Frédéric Bigey
French context:


- Laboratoire du Fractionnement et des Biotechnologies (LFB): private plasma fractionator with 100% public funds, has the obligation to fractionate the plasma collected by EFS.

- Increase of LFB demand since 2014, agreement up to 2020:

<table>
<thead>
<tr>
<th>LFB plasma demand</th>
<th>Global plasma volume (L)</th>
<th>additionnal plasmapheresis</th>
<th>% increase</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>TOTAL</td>
<td>Recovered</td>
<td>Apheresis</td>
</tr>
<tr>
<td>2016</td>
<td>854,500</td>
<td>600,443</td>
<td>254,057</td>
</tr>
<tr>
<td>2017</td>
<td>894,500</td>
<td>605,209</td>
<td>289,291</td>
</tr>
<tr>
<td>2018</td>
<td>934,500</td>
<td>592,747</td>
<td>341,753</td>
</tr>
<tr>
<td>2019</td>
<td>974,500</td>
<td>581,579</td>
<td>392,921</td>
</tr>
<tr>
<td>2020</td>
<td>991,500</td>
<td>570,623</td>
<td>420,877</td>
</tr>
</tbody>
</table>
EXPERIENCE OF GRAND EST

EFS

EFS Grand Est (GEST)

- Population 5 559 051 (= DK, 1/2 BE)
- 11 collection sites
- 375,000 donations/year
  (12.5% of national)

3 million donations/year
GENERAL ORGANIZATION

11 plasmapheresis sites

- Donations **targets** by sites, weekly follow-up
- **Multiple activities** on all the sites (WB, plasma, +/- platelets),
- **Multi-skilled staff**
- Dedicated plasmapheresis areas
- **Homogenous** range of apheresis **separators** in each site
  better safety and process control
- **1 nurse -> 4 apheresis separators**
TARGET ORGANIZATION : STRASBOURG

- 12 separators
- Large opening hours : 8 am – 8 pm (Mo-Fr), 8 – 12 am (Sa)
- Welcoming and comfortable environment
PLANIFICATION METHOD

- **Capacity** of each sites with **current ressources**
  opening hours/average donation time x number of separators
  average occupancy rate expected : 80%

- **Capacity** with possible **additionnal ressources**
  separators, opening hours, personal
  Efficiency balance

- **Donors** capacity

  **Recruitment** possibility, donation **frequency (loyalty)**,
  help of geo-business intelligence

- **Call center** capacity
  → Annual plan to increase plasmapheresis for each site
  Objective : 74,480 plasmapheresis in 2017
- Conversion from **mobile session**: a virtuous circle

- Conversion from **donor files** (call center)

- Conversion **on-site** from WB donors
PASSEZ À L’ACTION ET DONNEZ VOTRE PLASMA !


Mes coordonnées :
- Nom : [ ] Homme | [ ] Femme
- Prénom :
- Nom d’usage (maternel) :
- Nom de naissance :
- Adresse :
- Code postal :
- Ville d’habitation :
- Téléphone :
- Date de naissance :
- Email :

Mon profil :
- J’ai déjà donné mon sang : [ ] Oui | [ ] Non
- J’ai déjà donné mon plasma : [ ] Oui | [ ] Non

Je m’engage à donner mon plasma** :
Je demande à être appelé pour prendre rendez-vous pour un don de plasma. Mes préférences :
- Date :
- Heure :
- Commentaires :

** Service disponible dans les régions indiquées sur la carte.
** sous réserve de l’accord de la personne en charge de remettre la prélevement au don.

Vivez une nouvelle expérience ! Don de plasma
**PLASMA RECRUITMENT LEAFLET 2/2**

**LE PLASMA, QU'EST-CE QUE C'EST ?**
Le plasma est la partie liquide du sang dans laquelle circulent les cellules sanguines (globules rouges, globules blancs et plaquettes). Il contient des protéines d’un intérêt thérapeutique majeur pour de nombreux patients.

**POCHE DE PLASMA**
- Autres molécules 8%
- Écr 90%
- Protéines 6%

**Comment donner son plasma ?**
Vous pouvez choisir de donner exclusivement votre plasma en effectuant une « phlébotomie ». Grâce à cette technique, les différents composants du sang sont séparés à l’aide d’un automate qui recueille votre plasma et vous restitue vos globules rouges, globules blancs et plaquettes.

La phlébotomie permet de prélever plus de plasma que lors d’un don de sang.

**Qui peut donner son plasma ?**
Toute personne âgée de 18 à 65 ans reconnue apte à l’issue de l’évaluation préalable au don, il n’est pas nécessaire d’avoir déjà donné son sang pour faire un don de plasma.

Les personnes de groupe AB sont demandées universellement pour le plasma. En effet, leur plasma peut être transfusé à tous les patients. Seul 4 % des Français sont du groupe AB. Leur plasma est donc rare et précieux.

**SOYEZ INCOLLABLE SUR LE PLASMA 😄 !**
Le plasma peut suivre deux parcours différents. Selon les besoins du patient, il peut être administré par transfusion ou sous forme de médicaments.

**VOUS DONNEZ VOTRE PLASMA**

**LE PLASMA DÉLIVRÉ PAR TRANSFUSION**

**LE PLASMA DÉLIVRÉ SOUS FORME DE MÉDICAMENTS**

**Qui soigna-t-on ?**
Ce plasma est utilisé pour les patients atteints d’hémopathies, mais aussi pour ceux qui subissent une opération de neurochirurgie, de chirurgie cardiaque ou obstruée.

**Comment ça marche ?**
Pour être transfusé, le plasma doit passer par une étape de purification. Celle-ci consiste à conserver la poche de plasma dans l’attente d’un autre don qui doit avoir lieu 6 jours au moins après le don initial.

De J+41 à J+120 : c’est la bonne période durant laquelle vous pouvez vous fier à votre don initial ou en autre don.
Si les analyses de cet autre don sont conformes, votre don initial est alors disponible pour un patient.

Après J+120 : si vous n’êtes pas revenu sécuriser votre plasma, votre don initial servira à la fabrication de médicaments dérivés du plasma.

**Qui soigna-t-on ?**
Ces médicaments sont généralement utilisés pour les patients atteints de maladies chroniques. Certains d’entre eux ont des besoins toutes les 3 semaines, voire toutes les 3 ou 2 semaines.
Ils sont de plus en plus nombreux !

**Comment ça marche ?**
Les protéines sont extraites du plasma pour fabriquer des médicaments. Les trois principaux sont :
- **L’albumine** pour le prises en charge des grands brûlés, des lésions graves et des patients en réanimation.
- **Les immunoglobulines** pour les patients atteints de déficits immunitaires et de certaines maladies auto-immunes.
- **Les facteurs de coagulation** pour les maladies hémorragiques comme l’hémophilie.

**Vous êtes contre l’alcool et les tabacs ?**
Faites-en don !

**Action**
- Participation
- Patents
- Solidarité

**Vaccins contre l’hepatite B et le tétanos ?**
Faites-en don !

**You avez déjà donné des anticorps protecteurs contre ces maladies. Votre don de plasma est donc indisponible pour la fabrication de médicaments. Ces derniers sont utilisés pour le traitement préventif des personnes exposées à l’hépatite B (les nouveau-nés dont la mère est porteur de virus, les patients hémodialyse, ceux grattés du foie, ...) ou au tétanos.**

efs.sante.fr
Plasma donations in France and GEST, 2014 → 2017

Increase of plasmapheresis in France and GEST, 2014 - 2017

<table>
<thead>
<tr>
<th></th>
<th>France</th>
<th>GEST</th>
</tr>
</thead>
<tbody>
<tr>
<td>2014</td>
<td>168730</td>
<td>27120</td>
</tr>
<tr>
<td>2015</td>
<td>278750</td>
<td>49177</td>
</tr>
<tr>
<td>2016</td>
<td>336509</td>
<td>65192</td>
</tr>
<tr>
<td>2017</td>
<td>379284</td>
<td>71856</td>
</tr>
</tbody>
</table>

France : + 125%,

GEST : +165%, 19% of plasmapheresis in France

71,856 plasmapheresis in 2017 (96.5% of objective)
RESULTS

Plasma donations in GEST, by sites, 2014 → 2017

Increase plasmapheresis in GEST sites

Strasbourg : 18,576 - largest plasmapheresis site in France
<table>
<thead>
<tr>
<th>2017</th>
<th>Nb of plasma donors</th>
<th>GI</th>
<th>% new donors</th>
<th>LI</th>
<th>% plasma donors/all donors</th>
</tr>
</thead>
<tbody>
<tr>
<td>GEST</td>
<td>22138</td>
<td>0.63%</td>
<td>25%</td>
<td>3.64</td>
<td>12.6%</td>
</tr>
<tr>
<td>Strasbourg</td>
<td>5950</td>
<td>0.88%</td>
<td>28%</td>
<td>3.36</td>
<td>15.4%</td>
</tr>
</tbody>
</table>

**GI : Generosity Index = nb of donors/population between age 18-65**  
**LI : loyalty index = nb of donations / donors x year (excluding new donors)**

Best indicators for Strasbourg (except the LI)  
GI overall : 4.6 %
Plasma donors and distance to the site, Strasbourg example

<table>
<thead>
<tr>
<th>Distance to the site</th>
<th>5km</th>
<th>10km</th>
<th>15km</th>
<th>20km</th>
<th>25km</th>
<th>30km</th>
<th>40km</th>
<th>50km</th>
<th>60km</th>
<th>70km</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cumulative % of plasma donors</td>
<td>38%</td>
<td>51%</td>
<td>58%</td>
<td>66%</td>
<td>75%</td>
<td>81%</td>
<td>91%</td>
<td>98%</td>
<td>99%</td>
<td>99%</td>
</tr>
<tr>
<td>GI</td>
<td>0,94%</td>
<td>0,83%</td>
<td>0,97%</td>
<td>0,82%</td>
<td>0,74%</td>
<td>0,70%</td>
<td>0,50%</td>
<td>0,47%</td>
<td>0,39%</td>
<td>0,09%</td>
</tr>
</tbody>
</table>

1/3 of donors live in the urban area
1/2 of donors are within 10km
Still high GI up to 30km
Significant population contributing up to 50km

Recruitment/conversion: no stringent distance limit to be applied
GEOGRAPHY

Population and number of plasma donors, Strasbourg department (Bas-Rhin)

- Significant population of donors away from the site
- Recruitment targets: high population, low GI.
CALL CENTER SUPPORT

5 full-time-equivalent employees for Strasbourg site
- Conversion from donor files
  performance of phoning campaigns : 6,1%
- Conversion from WB donors on mobile session, call-back after registering
  overall performance : 4% of donors of mobile sessions
- Call-center reliability for appointments

30% of donors book on-site for their next donation
If Strasbourg performance rates applied to other sites of GEST :

- GI (recruitment, conversion) $\rightarrow$ 30,000 donors
- % plasma donors (conversion) $\rightarrow$ 26,000 donors
- With regional LI 3.6 : $\rightarrow$ 95,000 to 110,000 plasmapheresis/year

GEST maximum capacity with current ressources : 114,000 plasmapheresis/year

If Strasbourg performance applies at a national level in France

- GI : 0.31 to 0.88 $\rightarrow$ 1,000,000 plasmapheresis/year
- % plasma donors 11.5 to 15.4% $\rightarrow$ 1,000,000 plasmapheresis/year
SUCCESS FACTORS

- Multi-donation sites:
  - facilitates **on-site conversion** from WB donation candidates
  - **global information** of donors about blood products needs in a comprehensive voluntary unpaid national collection system.

- Multi-activity staff:
  - Knowledge of the different **types of donations**
  - Time during WB donation process allows **donor sensibilization** to plasma needs

- Team’s commitment

- Well structured **call center** activity

- Large **opening hours**

- **Volunteers** associations support
DIFFICULTIES AND ROOM FOR IMPROVEMENTS

- Heavy reliance to call center for donor loyalty → online booking to be developed

- Significant increase of plasmapheresis: conversion or direct recruitment?

- Direct recruitment would need larger public information on plasma needs as a national/european challenge

- Donor awareness about unpaid national donation system / international free trade for plasma-derived medicines: risk of demotivation?
- The development of a sustainable and efficient plasmapheresis program in a public unpaid collection system is possible

- The service to the donor is a key factor: comfortable and accessible venues, adapted opening hours, online booking system

- Achieving a higher level of plasmapheresis would need to clarify a national, then European, strategy towards self-sufficiency, making that question a public health issue.
Thank you for your attention!
Donor Motivation: EU Plasma Center Experiences

EDQM
January 2019
Yearly Overview 2005-2017

2017 - Collection Volumes (l)

Volume of plasma collected (liter)

Number of plasma collection centers

DE
AT
CZ & HU

Volume (l)
Center
Number of EPA plasma centers 2005 – 2017

EPA Plasma Collection Centers

2017: Centers

DE: 69
AT: 17
CZ&HU: 21
Some Realities of EU Plasma Collection

- Limitations on donor recruitment exist
- Donation numbers have been relatively flat or shrinking
- Changing demographics and trends shape different methods of donor communication
- Different member states sometimes have different requirements and approaches
- Donor motivation differs greatly not only among member states but among communities
Center Location and Awareness

- Center location is linked to demographic of donors.
- University towns (generally but not always) skew toward younger populations.
- Center’s popularity is also related to parking availability and transportation options.
- Many different tactics are used: social media, posters, website, flyers, radio advertising, campus adverts, mall adverts, city posters
- Most donors come in by word of mouth.
- Most donors come back because they’re treated well.
Donors represent diversity in a population and in an area.

An “average” age can be mid-30s, but many donors are both older and younger.

Generations in different segments respond differently to donation messages.

Humans are complex and have a mix of motivations and circumstances in life.
Donors and Centers

• Highly dependent on location, city, area, country.

• Some centers have young donor populations:
  – One example: 50% 18-25 y.o., 32% 25-36 y.o.
  – Another: 67% 18-29 y.o.

• Other centers are actively recruiting older (Gen X) donors.
Generational differences make for different marketing segments.

- Gen Z: mid-90s to mid-00s
- Gen Y (Millennial): early 80s to mid-90s
- Gen X: mid-60s to 1980
- Baby Boomer: 1945 to mid-60s

All have different expectations regarding donations.

Demographic make-up varies greatly by location.
Responding to Donor Segments

- **Gen Z:**
  - Oriented toward social media, mobile social media
  - Interested in what is “in it for them.”
  - Lower retention, lower center/brand loyalty
  - “Old advertising” doesn’t work

- **Gen Y/Millennial:**
  - More interested in social causes and values
  - Also oriented toward mobile platforms and social media.
  - More demanding of information, extras in-center

- **Gen X:**
  - Focused on individual achievement and goal-oriented
  - Responsive to several different advertising methods
  - Aware of center environment
  - Usually very busy schedules
  - Often a sought-after segment due to commitment and demographic under-representation

- **Baby boomer:**
  - Prefer greater routines and prefer to be able to plan
  - Classic media outreach
  - Tend to engage more with center staff and other donors
  - Responsive to promotional outreach

- **Tactics to attract donors change depending on where they are in life**
- **Centers and companies adjust systems and tactics**
Why donors donate

- Plasmapheresis can be uncomfortable
  - Personal and private questioning
  - Needlestick
  - Connected to a machine
  - AC/Saline

- Donors appreciate being saluted for their contributions.

- Donors also appreciate being a part of something that helps save lives.
General Challenges

- Crowded infosphere
  - Competitive attention attractors
- Recruitment challenges shift with fads and trends
  - Not just demographic
  - Environments and trends constantly evolving
  - Shrinking numbers of available donors
    - Time constraints
    - Awareness
    - Willingness
Tactics to improve donor retention

• Operational excellence
  – Treating donors fairly and well
  – Respectful of their time and lives
  – Attracting donors

• Recognizing donors for what they do

• Educate and inform donors about plasma and how it is used.
  – Patient group visits

• Understand that different donors have different motivations
Tactics for improvement

• Understand that different donors respond differently to channels and calls for donation.
  – Technology solutions abound for connecting to donors and potential donors
  – Streamlining donor processes using technology in-center

• Flexibility of opening hours to cater to different personal schedules.
  – Sometimes, requirements harm this need
Focus on the Patient

• Ultimately, the issue is that the world needs more plasma, and the only good way to make that happen is to collect more plasma. The one thing that we can all do right now is to encourage people to become regular plasma donors if there’s a collection center them.

  • John Boyle, CEO, IDF
THANK YOU
Grant Agreement 738145

TRANSfusion and transplantation
PrOtection and SElection of donors
TRANSPOSE

(TRANSfusion and transplantation: PrOtection and SElection of donors)

Marian van Kraaij, MD PhD
hematologist-transfusion medicine specialist
Director Units Transfusion Medicine and Donor Affairs, Sanquin Blood Supply
TRANSPOSE Programme Leader
The Netherlands
29 January 2019
Objectives

TRANSPOSE aims at a structured, alternative approach to construct risk-based Guidelines and a standard DHQ for the procedures used to collect SoHO, including the selection and protection of donors.

The objective of this action is:

• To collect and compare EU and national donor selection and protection criteria;
• To identify the information needed from donors or their families to allow the application of appropriate donor deferral or exclusion criteria for the protection of recipients; and
• To propose approaches to control and minimise these risks.
Substances of Human Origin (SoHO)

• Blood
• Plasma
• Tissues and Cells
• ART (assisted reproductive technology)

• Excluded: organs
Work Packages

There are three horizontal work-packages (WPs);

• Coordinating (WP 1),
• Disseminating (WP 2), and
• Evaluating the project (WP 3).

Four technical ones (WP’s 4-7) with specific deliverables and milestones
## Work Packages

<table>
<thead>
<tr>
<th>WP Number</th>
<th>WP Title</th>
<th>Lead Beneficiary</th>
</tr>
</thead>
<tbody>
<tr>
<td>WP1</td>
<td>Coordination of TRANSPOSE</td>
<td>Sanquin Blood Supply</td>
</tr>
<tr>
<td>WP2</td>
<td>Dissemination of the results of TRANSPOSE</td>
<td>Centro Nazionale Sangue</td>
</tr>
<tr>
<td>WP3</td>
<td>Evaluation of TRANSPOSE</td>
<td>Établissement Français du Sang</td>
</tr>
<tr>
<td>WP4</td>
<td>Inventory of Donor Selection &amp; Protection Practices</td>
<td>University of Cambridge</td>
</tr>
<tr>
<td>WP5</td>
<td>Development of Donor Selection &amp; Protection Guidelines</td>
<td>Region Hovedstaden Denmark</td>
</tr>
<tr>
<td>WP6</td>
<td>Development of a Standard Donor Health Questionnaire</td>
<td>University of Hamburg</td>
</tr>
<tr>
<td>WP7</td>
<td>Training Course/Workshop on the Use of the Guiding Principles</td>
<td>Établissement Français du Sang</td>
</tr>
</tbody>
</table>
Organisation technical WP’s (4-7)

• 5 subgroups with subgroup leaders per SoHO
  • Blood
  • Plasma (for transfusion and for fractionation)
  • Tissues
  • Stem cells and Cord blood
  • ART
Results up to now

- WP 2: Dissemination of results: website, flyers and newsletters
- WP 4: Inventory of donor selection and protection practices (finished)
- WP 5: Development of donor selection and protection guidelines (preliminary)
WP 4 (University of Cambridge)

Inventory of Donor Selection & Protection Practice per SoHO

• Identifying current system/ donor health questionnaire (DHQ)

• DHQ (based on in-depth interviews) were sent to 130 experts for comments
  • -> basis for an overarching DHQ

• Plasma specific (results from 6 countries/ regions):
  • separate questionnaire for plasma donation (collection through apheresis)
  • different risks for both recipient and donor as compared to whole blood
  • importance with regard to self-sufficiency of plasma collection within EU
WP 5 (Regio Hovedstaden Denmark)
Development of Donor Selection & Protection Guidelines

• Guiding principles for all SoHO
• Developing appropriate risk assessment tool to assess the level of (acceptable) risks
• Assessing all (potential) risks for donors and recipients per SoHO
  1. General health
  2. Risk behaviour, travel, transfusion transmittable infections (TTI)
  3. Diseases
Top risks of donation of plasma for fractionation/ transfusion (apheresis)

Donor risks:
• 1. Donor low on IgG and total protein
• 2. Relative overdraw of small/obese donors
• 3. Serious donor reactions (vasovagal, hematomas, nerve lesion etc.)
• 4. Repetitive exposure to large amounts of citrate (bone demineralization)
• 5. Repetitive exposure to plasticizers (DHEP)
• 6. Machine errors

Recipient risks:
• 7. Infections of plasma with (so far unknown) agents
How to proceed?

• Risk assessment (tool) per item regarding donor/recipient
• Severity of risk (grade 1-4) and imputability (NA, 0-3)
• Current evidence (literature search)

• -> Gaps: need for further evidence based research
• -> Recommendation: repeat risk assessment per SoHO every 2-3 years

• WP 5 will be finished April 2019: reports and scientific papers
• Input for DHQ (WP 6) and educational programme (WP7)
• Final results: March 2020
Thank you for your attention!

Acknowledgement:
Gaia Mori, Programme Office
Transpose Members

g.mori@sanquin.nl
transpose@sanquin.nl
RECOVERED PLASMA FOR FRACTIONATION

Session on:

Efficiency of collection practices - how can obstacles be overcome?

Dr. René Büchel
Head 3rd Party Plasma Europe
Baxalta GmbH, Zug Switzerland
The goal of today’s speech is to discuss:

1. How could recovered plasma be used to its full potential for fractionation
2. Proposals for a way forward to intensify recovered plasma collection
3. The obstacles to strategic independence of plasma for fractionation in Europe
4. Whether the EU legislation itself could be perceived as a barrier to expand the availability of plasma for fractionation
1) How could recovered plasma be used to its full potential for fractionation

The reality is that in 2018, Recovered Plasma (RP) represents only 15% of the Plasma for Fractionation (PfF) used worldwide.
Europe has the highest portion of RP been fractionated!

Limited room for improvement!
Estimated blood donations by WHO region, 2013

<table>
<thead>
<tr>
<th>Region</th>
<th>Estimated whole blood donations (millions)</th>
<th>Estimated apheresis donations (millions)</th>
<th>Total (millions)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Africa</td>
<td>5.6</td>
<td>0.03</td>
<td>5.6</td>
</tr>
<tr>
<td>Americas</td>
<td>20.4</td>
<td>2.0</td>
<td>22.4</td>
</tr>
<tr>
<td>Eastern Mediterranean</td>
<td>9.9</td>
<td>0.04</td>
<td>9.9</td>
</tr>
<tr>
<td>Europe</td>
<td>26.5</td>
<td>6.1</td>
<td>32.5</td>
</tr>
<tr>
<td>South-East Asia</td>
<td>16.6</td>
<td>0.06</td>
<td>16.7</td>
</tr>
<tr>
<td>Western Pacific</td>
<td>21.6</td>
<td>3.7</td>
<td>25.3</td>
</tr>
<tr>
<td>Global (rounded totals)</td>
<td>100.6</td>
<td>11.9</td>
<td>112.5</td>
</tr>
</tbody>
</table>

Global status report on blood safety and availability 2016!!

Partly incorrect data. Further, data shows huge discrepancies amongst regions. Donations in Asia ≠ Europe (average 300 ml versus 500 ml)
9 mio l unused RP as claimed by WHO (really true? Why?)
1) How could recovered plasma be used to its full potential for fractionation

Despite 4 mio RP, Europe is dependant from US source plasma (up to 5 mio l / 28% of IgG WW consumption in 2016 acc. to MRB = 14mio l)

This volume cannot be covered by RP!
1) How could recovered plasma be used to its full potential for fractionation
2) Proposals for a way forward to intensify recovered plasma collection

Blood collections have declined in all developed countries because of patient blood management (therefore the availability of RP as PfF has declined too)

In Europe only few countries destroy their plasma, mainly due to political or regulatory reasons (see later), therefore, EU RP is more or less optimally used

And what about the rest of the World: Annex 14 is a wall against importing any plasma from outside the EU (US excepted!), or at least is wrongly interpreted as such by regulators room for improvement.
3. The obstacles to strategic independence of plasma for fractionation in Europe

In the past ten years, source plasma collections in the United States and in China have grown the fastest, but Europe has been slowly catching up within a limited number of countries.
3. The obstacles to strategic independence of plasma for fractionation in Europe

- The EU has as many collection models as countries
- Gvt. controlled collection organizations are by far not self-sufficient, countries with open market are self-sufficient
- Non-for profit organizations in most cases not interested in producing plasma
- Most countries import plasma-derived medicinal products from international sources to meet the needs of patients instead of investing in own infrastructure
- EU does not support industry’s efforts (at least until now)
4. Whether the EU legislation itself could be perceived as a barrier to expand the availability of plasma for fractionation

- The annual volume of a plasma donation allowed per donor is the main factor differentiating the ability of a country to supply PfF
- Missing an EU regulatory framework allowing local plasma production by apheresis
- Private activities prohibited or difficult due to regulatory gaps
- Existence of artificial trade barriers (e.g. import/export of plasma prohibited)
- Nationally regulated blood system conflict with international rules or guidelines (See next slide)
- And last but not least: EU PMF is a bureaucratic barrier to new suppliers (eg.: plasma from a FTBD not good enough despite the blood was transfused!!)
RECOVERED PLASMA FOR FRACTIONATION

COLLECTION AND TESTING
- 2002/98/EC
- Pharm. Eur.
- 2004/33/EC
- 2005/61/EC
- 2005/62/EC
- CHMP/BWP/706271/2010
- Guidelines EU PMF & Epidemiology
- National Laws
- FDA regulations
- EU GMP Guide & Annex 14

FRACTIONATION
- 2001/83/EC
- Pharm. Eur.
- 2003/94/EC
- EU PMF & Epidemiology Guidelines
- National Laws
- EU GMP Guide & Annex 14
- FDA regulations

MEDICINAL PRODUCTS
- 2003/94/EC
- Pharm. Eur.
- National Laws
- FDA regulations
- CHMP/BWP/706271/2010
- EU GMP Guide & Annex 14
- EC Procedure OCABR: Batch Release

QUALITY MANAGEMENT & GMP
1. Open up more plasma centers in Europe is a must to reduce US dependency
2. Allow public and private centers to compete
3. Increase plasmapheresis as the primary method to collect plasma for manufacturing
4. Stop creating artificial regulatory barriers to import/export of plasma
5. Simplifying EU PMF procedure which lost its original purpose
6. Increase quality of recovered plasma still needed in some countries
7. Stop discarding recovered plasma for political reasons and regulatory reasons despite blood is transfused !!
German Red Cross (DRK) in Bavaria (BRK)- with both Whole Blood and Plasma Centers

Dr. Franz Weinauer
Die DRK-Blutspendedienste

- DRK-Blutspendedienst Nord-Ost
- DRK-Blutspendedienst Mecklenburg-Vorpommern
- DRK-Blutspendedienst NSTOB
- DRK-Blutspendedienst West
- DRK-Blutspendedienst Baden-Württemberg - Hessen
- Blutspendedienst des Bayerischen Roten Kreuzes (gemeinnützige GmbHs)
Blood and Plasma Centers of the BRK
29,370 units of plasma were donated in Bavaria in 2017.

TODAY: PLASMA DONATION

2,242 people were willing to donate plasma in Bavaria in 2017 on the specified dates.

487,535 units of blood were donated in Bavaria in 2017.

∅ 2 units of blood on average were given by registered blood donors in 2017.

43 years is the average age of a male person donating blood.

40 years is the average age of a female person donating blood.
Durchschnittsalter WB donors Bayern

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-25</td>
<td>19,90%</td>
</tr>
<tr>
<td>26-35</td>
<td>18,80%</td>
</tr>
<tr>
<td>36-45</td>
<td>16,30%</td>
</tr>
<tr>
<td>46-55</td>
<td>24,90%</td>
</tr>
<tr>
<td>56-65</td>
<td>16,00%</td>
</tr>
<tr>
<td>&gt;65</td>
<td>4,10%</td>
</tr>
</tbody>
</table>

Durchschnittsalter Plasmapendel

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-25</td>
<td>65,00%</td>
</tr>
<tr>
<td>26-35</td>
<td>22,60%</td>
</tr>
<tr>
<td>36-45</td>
<td>4,10%</td>
</tr>
<tr>
<td>46-55</td>
<td>5,50%</td>
</tr>
<tr>
<td>56-65</td>
<td>2,60%</td>
</tr>
<tr>
<td>&gt;65</td>
<td>0,30%</td>
</tr>
</tbody>
</table>
### Donation Frequency WB and Plasma at the BRK Blood Bank

Average number of donations per year (2017)

<table>
<thead>
<tr>
<th>Whole blood donors*</th>
<th>Plasma donors **</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1 - 10</td>
</tr>
<tr>
<td>48,5 %</td>
<td>74,7 %</td>
</tr>
<tr>
<td>2</td>
<td>11 – 20</td>
</tr>
<tr>
<td>24,4 %</td>
<td>14,6 %</td>
</tr>
<tr>
<td>3</td>
<td>21 - 30</td>
</tr>
<tr>
<td>15,6 %</td>
<td>5,5 %</td>
</tr>
<tr>
<td>4</td>
<td>31 - 40</td>
</tr>
<tr>
<td>8,6 %</td>
<td>3,1 %</td>
</tr>
<tr>
<td>5</td>
<td>41-50</td>
</tr>
<tr>
<td>2,2 %</td>
<td>1,8 %</td>
</tr>
<tr>
<td>6</td>
<td>&gt; 51</td>
</tr>
<tr>
<td>0,6 %</td>
<td>0,1 %</td>
</tr>
</tbody>
</table>

* N = 487,535  
**N= 29,370 (center Würzburg)
Donor Types-Plasma vs WB at the Bavarian Red Cross Blood Centers

- **WB**
  - age (average: m 40, f 43)
  - male 54% female 46%
  - non remunerated
  - altruistic
  - donation as social event
  - most donors in rural areas
  - low frequency of donation (2/yr)

- **Plasma**
  - „younger“ (30y)
  - male 41% female 59%
  - remunerated
  - „do ut des“, but they see also the need
  - donors predominantly in cities (like PC‘s are)
  - „higher“ frequency of donation (10 / y)
Crowding out of whole blood donors to plasma??

At present it is not very likely seeing the differences in both groups

Figures after the opening of three plasma centers show no negative influence on WB donations in that particular area (no difference in the year before, compared to the years after opening)
Blood donation in the INGOLSTADT area 01/1989 until 10/2018

Opening of the plasma center Ingolstadt 1990
Blood donation in the city of Bayreuth 01/2004 until 11/2018

Opening of the plasma center Bayreuth 2005
<table>
<thead>
<tr>
<th>Year</th>
<th>Geplant</th>
<th>Anwesend</th>
<th>TAT</th>
</tr>
</thead>
<tbody>
<tr>
<td>01/2015</td>
<td>150</td>
<td>120</td>
<td>30</td>
</tr>
<tr>
<td>02/2015</td>
<td>150</td>
<td>120</td>
<td>30</td>
</tr>
<tr>
<td>03/2015</td>
<td>150</td>
<td>120</td>
<td>30</td>
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<td>04/2015</td>
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<td>120</td>
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<td>05/2015</td>
<td>150</td>
<td>120</td>
<td>30</td>
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<tr>
<td>06/2015</td>
<td>150</td>
<td>120</td>
<td>30</td>
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<tr>
<td>07/2015</td>
<td>150</td>
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<td>08/2015</td>
<td>150</td>
<td>120</td>
<td>30</td>
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<tr>
<td>09/2015</td>
<td>150</td>
<td>120</td>
<td>30</td>
</tr>
<tr>
<td>10/2015</td>
<td>150</td>
<td>120</td>
<td>30</td>
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<tr>
<td>01/2016</td>
<td>150</td>
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<td>02/2016</td>
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</tr>
</tbody>
</table>

**March 2017:** approx. 1,800 WB donors BG AB asked to donate plasma

**Opening plasma center Würzburg October 2016**
Crowding out?

In March 2017 approx. 2,000 WB-donors in the area (30 km) of Würzburg with blood group AB were informed about the plasma donation center and invited to come

Result:

- After 2 weeks 2 donors responded
- A week later another 3 donors responded
- Each of those 5 donors gave 1 donation
- all returned to WB donation and stopped donating plasma
Released Packed Red Cells 2009-2017 (PEI data)
(1 Million x 280 ml plasma units less in 2017 compared to 2009)
Will there be enough plasma?
Plasma donation in Europe 2017 (data MRB)

<table>
<thead>
<tr>
<th>Country</th>
<th>Recovered</th>
<th>Apheresis</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Austria</td>
<td>100</td>
<td>555</td>
<td>655</td>
</tr>
<tr>
<td>Belgium</td>
<td>120</td>
<td>-</td>
<td>120</td>
</tr>
<tr>
<td>Bulgaria</td>
<td>15</td>
<td>-</td>
<td>15</td>
</tr>
<tr>
<td>Croatia</td>
<td>25</td>
<td>-</td>
<td>25</td>
</tr>
<tr>
<td>Czech Republic</td>
<td>60</td>
<td>421</td>
<td>481</td>
</tr>
<tr>
<td>Denmark</td>
<td>44</td>
<td>39</td>
<td>83</td>
</tr>
<tr>
<td>Estonia</td>
<td>11</td>
<td>-</td>
<td>11</td>
</tr>
<tr>
<td>Finland</td>
<td>42</td>
<td>-</td>
<td>42</td>
</tr>
<tr>
<td>France</td>
<td>632</td>
<td>260</td>
<td>892</td>
</tr>
<tr>
<td>Germany</td>
<td>985</td>
<td>1,977</td>
<td>2,962</td>
</tr>
<tr>
<td>Greece</td>
<td>2</td>
<td>-</td>
<td>2</td>
</tr>
<tr>
<td>Hungary</td>
<td>79</td>
<td>323</td>
<td>402</td>
</tr>
<tr>
<td>Italy</td>
<td>620</td>
<td>210</td>
<td>830</td>
</tr>
<tr>
<td>Latvia</td>
<td>8</td>
<td>-</td>
<td>8</td>
</tr>
<tr>
<td>Lithuania</td>
<td>11</td>
<td>3</td>
<td>14</td>
</tr>
<tr>
<td>Netherlands</td>
<td>92</td>
<td>234</td>
<td>327</td>
</tr>
<tr>
<td>Norway</td>
<td>54</td>
<td>10</td>
<td>64</td>
</tr>
<tr>
<td>Poland</td>
<td>229</td>
<td>84</td>
<td>314</td>
</tr>
<tr>
<td>Portugal</td>
<td>90</td>
<td>-</td>
<td>90</td>
</tr>
<tr>
<td>Serbia</td>
<td>10</td>
<td>-</td>
<td>10</td>
</tr>
<tr>
<td>Slovakia</td>
<td>20</td>
<td>-</td>
<td>20</td>
</tr>
<tr>
<td>Slovenia</td>
<td>11</td>
<td>-</td>
<td>11</td>
</tr>
<tr>
<td>Spain</td>
<td>353</td>
<td>20</td>
<td>373</td>
</tr>
<tr>
<td>Sweden</td>
<td>98</td>
<td>25</td>
<td>123</td>
</tr>
<tr>
<td>Switzerland</td>
<td>70</td>
<td>5</td>
<td>75</td>
</tr>
<tr>
<td>Other Europe</td>
<td>30</td>
<td>-</td>
<td>30</td>
</tr>
</tbody>
</table>

Sub-total Europe 3,811 4,166 7,977
Is there a need to remunerate?
Donor „burden“ is different

WB donation: no
- Bavarian RC Blood service comes to place where the donor lives
- Donation time is short
- Self sufficiency guaranteed without remuneration (or major gifts)
- Needs of the patients are met

Plasma donation: currently: yes
- Donor is required to come to the center (has travel expenses, needs time)
- Donation takes more time (30min)
- Self sufficiency currently only achieved in countries where compensation is introduced
- Ethical principles of donation?
- From an ethical point of view the needs of the patients have also to be considered (but: what is the real need: is off label use a cause for shortage?)
Conclusions

- Notable differences exist in WB vs plasma donors (age, motivation, frequency)

- Currently there is no crowding out of WB donors to plasma donations in Bavaria

- There is some „cross-donation“, but the typical plasma donor is not willing to give WB without compensation and WB donors are not attracted by plasma donation

- Plasma programs intended to reach self sufficiency for plasma for fractionation without remunerating the donor are very difficult to achieve.
Denmark:
Blood Establishments Efforts in Order to Expanse Plasma Collections

Jørgen Georgsen & Kjell Titlestad
South Danish Transfusion Service

EDQM Plasma Supply Management
Strasbourg January 29-30, 2019
Obstacles to Independence of Plasma for Fractionation in Europe

• Unpaid Donor Availability
  – Donor Organizations
  – Blood Establishments
  – National Blood Services/National Authorities

• Change of Operation
  – Blood Establishments

• Costs
  – Number of hours work per week and year
  – National level of general costs and salaries

• Legislation
  – EU Organs
  – National Authorities
The Danish Background

- National contract with international plasma fractionator
- 80 tons recovered plasma
Then There Was a Decrease....
Mind the Gap...

• In 2013 decision by the health authorities to produce plasma by plasmapheresis to fulfill the contract
Then There Was an Increase...

Use of IG in Denmark; pop. 5.8 mio.
...and an Even Bigger Gap!

- Self-sufficiency with IVIG
  - 40 ton recovered
  - 80 ton source (≈ 110,000 collections)

- Self-sufficiency with IVIG & SCIG
  - 40 ton recovered
  - 170 ton source (≈ 240,000 collections or 180,000 more than present)
Unpaid Donor Availability
Is it possible with unpaid donors?

Factor VIII
30% of RBC discarded
Change of Operation
Beginner’s Lesson # 1: Plasmapheresis Collection is Very Different from WB Collection

- Procedures
- Registrations
- Blood grouping
- Haemoglobin measurement
- Body weight > 60 kg
- Number of donors handled by one staff member
Beginner’s Lesson # 2:
Do Not Standardize Volume to be Collected

• Minimal volume 600 ml
• Every ml > 600 is pure ”plasma profit”
Simple Rules

- 60-70 kg: 600 ml
- 70-80 kg: 700 ml
- > 80 kg and male: 800 ml

- Freezers not capable of freezing 800 ml bags (space!) 😞 [Now solved]
Beginner’s lesson # 3: Simplify Data Collection

• No paper, all data captured electronically
• Reading of 46 bar codes (nice to have) changed to reading of 13 bar codes
• Think need to have
• Create batch of consumerables for apheresis harness
## Results in Numbers (One Centre)

<table>
<thead>
<tr>
<th>Year</th>
<th>Procedures (including plasma for transfusion)</th>
<th>Average weight (kilograms)</th>
<th>Yield (tons)</th>
<th>Yield/machine (tons)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2015</td>
<td>10,249 (10,674)</td>
<td>0.624</td>
<td>6.399</td>
<td>0.582</td>
</tr>
<tr>
<td>2016</td>
<td>18,136 (18,294)</td>
<td>0.615</td>
<td>11.158</td>
<td>1.014</td>
</tr>
<tr>
<td>2017</td>
<td>18,026 (18,861)</td>
<td>0.646</td>
<td>11.657</td>
<td>1.060</td>
</tr>
<tr>
<td>2018</td>
<td>18,819 (19,498)</td>
<td>0.658</td>
<td>12.388</td>
<td>1.126</td>
</tr>
<tr>
<td>Goal</td>
<td>20,200</td>
<td>0.680</td>
<td>13.7</td>
<td>1.245</td>
</tr>
</tbody>
</table>

- 11 beds
- Opening hours:
  - Monday-Thursday: 7-20, first donor 7:15, last donor 19:00
  - Friday: 7-16, first donor 7:15, last donor 15:00
  - Saturday-Sunday: Closed
Outstanding Issues

• Still to small – need 25 beds/centre for optimal efficiency
• Location: Staff also do WB collection and therapeutic apheresis procedures
  – Flexibility ↑
  – Interference with productivity ↓
• Ergonomics
• Service by the vendor
Costs
Productivity

- Productivity per hour 😊
- Production per FTE
  - Working hours per week 34.5 hours
  - Holidays and public holidays 6 weeks + 10 days
- Production and cost per FTE
- General level of costs
Denmark was the most expensive EU Member State for food and non-alcoholic beverages and Sweden for clothing in 2017.

**Price level index for household final consumption expenditure (EU-28=100), 2017**

*Source: Eurostat (online data code: prcppplnd)*

This article presents the most recent analysis of price levels for consumer goods and services in the European Union (EU), focusing on price level indices (PLIs), which provide a comparison of countries' price levels relative to the EU average and are calculated using purchasing power parities.
Costs

• Procurement of scale
  – Equipment
  – Harness
  – Test kits

• Role for European Blood Alliance
Legislation

- Judgement in the Medisanus vs. Slovenia case
- Donors → fractionator → patients deemed illegal by the government’s lawyer
- Contract terminated before expiration
- Donors → fractionator → patients
- Donors → fractionator → patients
- Harder to recruit donors – they see it as commercialization
Legislation

• Judgement in the Medisanus vs. Slovenia case

• D donors → fractionator → E patients
deemed illegal by the government’s lawyer

• Contract terminated before expiration

• D donors → fractionator → E patients

• E donors → fractionator → D patients

• Harder to recruit donors – they see it as commercialization
Legislation

- Judgement in the Medisanus vs. Slovenia case
- Donors → Fractionator → Patients deemed illegal by the government’s lawyer
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- Donors → Fractionator → Patients
- Donors → Fractionator → Patients
- Harder to recruit donors – they see it as commercialization
Legislation

• Judgement in the Medisanus vs. Slovenia case

• \[\text{denmark} \rightarrow \text{fractionator} \rightarrow \text{denmark patients}\]
deemed illegal by the government’s lawyer

• Contract terminated before expiration

• \[\text{denmark} \rightarrow \text{fractionator} \rightarrow \text{united nations patients}\]

• \[\text{united nations} \rightarrow \text{fractionator} \rightarrow \text{denmark patients}\]

• Harder to recruit donors – they see it as commercialization
Legislation

• Belgium and Italy have succeeded to continue with contract fractionation and thereby a national self-sufficiency programme

• Statement or Guidance needed from the Commission: What is right? What is possible?
Obstacles to Independence of Plasma for Fractionation in Europe

- **Unpaid Donors**
  - Donor Organizations
  - Blood Establishments
  - National Blood Services/National Authorities
  - *Is possible*

- **Change of operation model**
  - Blood Establishments
  - *Can be done*

- **Costs**
  - Number of hours work per week and year
  - National level of general costs and salaries
  - *Unchangeable conditions*

- **Legislation**
  - EU Organs
  - National Authorities
  - *Change or interpretation by the Commission*
200 Donations Celebrated
The rationale behind German guidelines on donor plasmapheresis

Germany: regulation on minimal IgG level for individualised donor management + current changes in the volumes and donation intervals

Peter Hellstern
Center of Hemostasis and Thrombosis Zurich
Zurich, Switzerland
• Present regulations Europe – Germany – USA
• Cornerstones of donor safety in the German Guidelines 2017
• Early studies on donor safety and intensity of plasma donation → USA
• Study on intensified plasmapheresis (SIPLA) and SIPLA II → Germany
• Further recent studies on donor safety → Germany
• German donor management, IgG levels, volumes, and donation intervals
• Conclusions
### Plasma donation – current regulations

<table>
<thead>
<tr>
<th></th>
<th>Germany 2017</th>
<th>Europe 2017</th>
<th>USA since 1992</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maximum per donation, ml</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>50 - 60 kg</td>
<td>50 - 60 kg</td>
<td>650</td>
<td>50 – 67 kg</td>
</tr>
<tr>
<td>60 - 70 kg</td>
<td>60 - 70 kg</td>
<td>750</td>
<td>68 – 79 kg</td>
</tr>
<tr>
<td>70 kg</td>
<td>70 kg</td>
<td>850</td>
<td>&gt;79 kg</td>
</tr>
<tr>
<td>Donation frequency</td>
<td>Twice weekly</td>
<td>Twice weekly</td>
<td>Twice weekly</td>
</tr>
<tr>
<td>Maximum per year</td>
<td>60</td>
<td>33</td>
<td>104</td>
</tr>
<tr>
<td>Minimum IgG, g/l</td>
<td></td>
<td></td>
<td>Serum electrophoresis</td>
</tr>
<tr>
<td>Every 5th donation</td>
<td>6.0</td>
<td>6.0</td>
<td>every 4 months</td>
</tr>
<tr>
<td>Minimum total protein, g/l</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Every 5th donation</td>
<td>60</td>
<td>60</td>
<td>60</td>
</tr>
<tr>
<td>Hemoglobin, g/l</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>♀ 120, ♂ 135</td>
<td>♀ 125, ♂ 135</td>
<td></td>
<td>125</td>
</tr>
</tbody>
</table>
Plasma donations of 500 - 1000 ml per session twice weekly over up to 3 years well tolerated

No plasma protein depletion.

- Kliman, 1964; n = 21
- Simson, 1966; n = 7
- Cohen & Oberman, 1970; n = 4
- Salvaggio, 1971; n = 95
- Shanbrom, 1972; n = 74
- Friedman, 1975; n = 41

However: The intensity of plasmapheresis is limited by the donors’ ability to restore their plasma proteins, particularly IgG.
Prospective identification of dropout reasons

Is intensified plasma donation safe?

- 50-70 kg → 750 ml
  >70 kg → 850 ml
- Up to 60 donations/year, up to twice weekly
- Every 5th donation IgG ≥ 5.8 g/l, TP ≥ 60 g/l
  Hb ≥ 115 g/l with every donation
- 3,783 donors, observation 3 years
Study on intensified plasmapheresis (SIPLA)

1 year at 35-38 750-ml plasma donations ml

Arm I <70 kg
750 ml per session

Year 1
Year 2
Year 3

Maximum 60 donations per year

Arm II >70 kg
850 ml per session

Year 1
Year 2
Year 3
SIPLA outcome after 3 years:

- Regular end: 923 (25%)
- Socioeconomic: 607 (16%)
- Medical, no SIPLA relation: 393 (10%)
- Medical, SIPLA relation: 1860 (50%)
Dropouts for SIPLA-related medical reasons

- Low IgG*: 469 (77%)
- Low TP*: 54 (9%)
- Low Hb*: 78 (13%)
- Others: 6 (1%)

*No normalization within 5 weeks after last donation
<table>
<thead>
<tr>
<th>Variable</th>
<th>Hazard ratio</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Higher initial IgG</td>
<td>0.1 (0.0-0.2)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Age, per 10 years</td>
<td>0.8 (0.7-0.9)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Male sex</td>
<td>0.6 (0.5-0.7)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Days between 2 donations</td>
<td>0.5 (0.4-0.6)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Body weight, per 10 kg</td>
<td>1.0 (0.9-1.1)</td>
<td>n.s.</td>
</tr>
<tr>
<td>Higher initial total protein</td>
<td>1.1 (0.9-1.4)</td>
<td>n.s.</td>
</tr>
<tr>
<td>Higher initial Hb</td>
<td>0.8 (0.6-1.2)</td>
<td>n.s.</td>
</tr>
<tr>
<td>ml plasma/kg b.w./session</td>
<td>1.4 (1.0-2.1)</td>
<td>n.s.</td>
</tr>
</tbody>
</table>
### Main differences between SIPLA and SIPLA II

<table>
<thead>
<tr>
<th></th>
<th>SIPLA</th>
<th>SIPLA II</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Inclusion</strong></td>
<td>Experienced plasma donors</td>
<td>All</td>
</tr>
<tr>
<td><strong>Type of donation</strong></td>
<td>Plasma only</td>
<td>All types</td>
</tr>
<tr>
<td><strong>Limit IgG, g/l</strong></td>
<td>5.8</td>
<td>6.0</td>
</tr>
<tr>
<td><strong>Limit Hb, g/l</strong></td>
<td>115</td>
<td>♀ 125, ♂ 135</td>
</tr>
<tr>
<td><strong>Donation volume below 60 kg of b.w.</strong></td>
<td>750</td>
<td>700</td>
</tr>
<tr>
<td><strong>Exclusion</strong></td>
<td>No donation within 5 weeks</td>
<td>No donation within 10 weeks or longer, e.g. socioeconomic</td>
</tr>
</tbody>
</table>
SIPLA II results

70,000 donations over 23 months, 42% females

IgG and TP below thresholds

- IgG 6.7% of tested donations, at least once in 27% of donors
- TP 6.6% of tested donations, at least once in 25% of donors

Total and severe vasovagal and hypotonic reactions

<table>
<thead>
<tr>
<th>Conditions</th>
<th>Donations</th>
<th>Total, %</th>
<th>Severe, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kiessig S 2013, prospective</td>
<td>SIPLA II</td>
<td>70,000</td>
<td>0.22</td>
</tr>
<tr>
<td>Diekamp U 2014, retrospective</td>
<td>Germany 2010</td>
<td>1,107,846</td>
<td>0.51</td>
</tr>
</tbody>
</table>
Why IgG $\geq$ 6.0 g/l?

- Lower limit of IgG reference range in healthy adults: 6.0 – 8.5 g/l
- 8 textbooks

IgG level and risk of pneumonia and other infections in primary immunodeficiency syndromes

- Inverse correlation between IgG trough levels and rate of bacterial infections between 0 and 10 g/l

- IgG replacement, minimum IgG trough target level 5 g/l, better > 6.0 g/l or greater
IgG levels < 6 g/l in plasma donations according to the 2010 German Guidelines Möller Anke, Dissertation 2014

1293 donations with IgG < 6 g/l
Median 5.5; min – max, 2.1 – 5.9

- IgG < 5.0 g/l  n=85  6.50%
- IgG < 4.0 g/l  n=5   0.38%
- IgG < 3.0 g/l  n=2   0.15%
IgG ≥ 6.0 g/l every 5th donation

IgG in serum but not in product plasma

The result must be available before the next donation

IgG < 6.0 g/l → next donation ≥ 2 weeks

IgG 3 times < 6.0 g/l → donor to be excluded permanently

Donor safety – IgG
German Guidelines 2017
Before 2017

- IgG < 6.0
- Extend time interval

German guidelines 2017

- IgG < 6.0
- Extend time interval by at least 2 weeks
- Permanent exclusion
Why IgG in serum?

Determination of IgG in product plasma (PP)

- Local validation, IgG serum/IgG PP ratios from donors
- Confidential survey in 2014 in 8 plasma center companies
- Ratios between 1.1 and 1.32
- Ratios: Strong interindividual variation
- Ratios: Depend on hematocrit and on duration of the donation procedure.

<table>
<thead>
<tr>
<th>IgG serum/IgG PP</th>
<th>IgG determined in PP g/l</th>
<th>Calculated serum IgG g/l</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.1</td>
<td>5.4</td>
<td>6.0</td>
</tr>
<tr>
<td>1.32</td>
<td>4.5</td>
<td>6.0</td>
</tr>
</tbody>
</table>
Why donation volumes including citrate?

The individual donation volume without citrate anticoagulant cannot be determined exactly.

<table>
<thead>
<tr>
<th>Center</th>
<th>Ratio IgM serum/IgM PP</th>
<th>Volume excluding citrate, ml</th>
<th>Volume including citrate, ml</th>
</tr>
</thead>
<tbody>
<tr>
<td>Center 1</td>
<td>1.09</td>
<td>650</td>
<td>700</td>
</tr>
<tr>
<td>Center 2</td>
<td>1.27</td>
<td>650</td>
<td>825</td>
</tr>
</tbody>
</table>

PP, product plasma
Why Hb 120 g/l in females?

- Lower Hb reference range limit in females 120 g/l
  Beutler E & Waalen J. Blood 2006;197:1747

- In contrast to whole blood donation, no significant loss of RBC if the
device is rinsed and the suspension reinfused at the end of the session

- SIPLA II
  Hb <125 g/l but ≥120 g/l 3.9% of tested donations in 21% of females
  Hb <120 g/l 0% of tested donations in females
IgG depletion limits the intensity of plasma donation → individual donation intervals

Close monitoring

- Every 5th donation
- Lower limit of the reference range → 6.0 g/l
- Determination in serum, not in product plasma
- Results have to be available before the next donation
- IgG below 6 g/l → prolong donation interval
- IgG below 6 g/l 3 times → permanent exclusion from plasma donation
Thanks for listening
NEW REGULATION FOR PLASMAPHERESIS DONORS
ONE WHOLE BLOOD DONATION PER YEAR
PLUS REGISTRY

Klara Baroti-Toth, Sandor Nagy
Plasma Supply Management, EDQM,
Hungarian regulation on blood supply

EU

98/2002/EC
33/2004/EC
61/2005/EC
62/2005/EC

Hungary

439/2015. (XII. 28.) Korm. Government decree

3/2005 (II.10) EüM r.
44/2005 (X. 19.) EüM r.
60/2003. (X. 20.) ESzCsM r.

2001/83/EC
Guide to the preparation, use and quality assurance of Blood Components
Recommendation No.R(95)15, EDQM, Strasbourg

Other important aspects
- Council of Europe/European Directorate for Quality of Medicines/European Pharmacopeia (CoE/EDQM/Ph.Eur.)
- European Medicines Agency (EMA)
- National Competent Authorities (NCA)
- Pharmaceutical Inspection Convention/Pharmaceutical Inspection Co-operation Scheme (PIC/S)
439/2015. (XII. 28.) government decree

has declared:

eg. National self-sufficiency,
    Stabile and Labile blood products,
    National blood stock,
    Industrial plasma,
    Hospital blood stock, etc.
Goals of the decree

The Hungarian National Blood Transfusion Service (HNBTS) is

- responsible for the blood supply in Hungary, coordinates the blood collection based on the annual plan,

- maintains and improves the donor register with cross deferral register covered the donor data with plasmapheresis centres.

To improve the attitude of the plasmadonors into the whole blood donation, so the plasma centres monitorize their donors’ whole blood donation (the minimum request once whole blood donation per year).
Goal of the contract among the HNBTS and plasmapheresis centres

To be safer procedure for the donors (with same requirements) and same quality of the recipients.

To prepare a unique donor register, with cross deferral register (The validation periode should be finalized at the end of March 2019.).

To prevent the TTI.

To find the donors to give blood again or at first time.

Every 6 month they should send their procedure’s data (it is confidential), but their donor deferral riports are implemented into the eProgesa, unique donor register to improve the blood safety.

To prepare a max. limit for donor expenses in the plasma centres.
Collected Whole blood

HUNGARIAN NATIONAL BLOOD TRANSFUSION SERVICE
Whole blood donors

년도 |Nr Donor
---|---
2010 | 269,874
2011 | 276,831
2012 | 276,810
2013 | 269,816
2014 | 267,457
2015 | 263,597
2016 | 261,761
2017 | 253,217
2018 |
Advantage of the National Donor Deferred Registry (NDDR)

- Code (HNBTS) of Deferral
- Registering of date,
- Start of date,
- End of date

Filtration in the data
- Number of Health Insurance, this a key ID Nr
- Date of birth,
- Gender,

Communication through
- website
- API (application programming interface) or web service
Post Donation Information from the plasmapheresis centres
(total donor number is confidential)

- CJD: 0 (2018) vs. 1 (2017)

The total donor number is confidential.
Deferrals of plasma donors

We could find some donors who give plasma products in 2 or 3 plasma centres parallel (4/2017.; 2/2018.)

In the database of the HNBTS (eProgesa) 13 (2017.) and 20 (2018.) plasma donors have been deferred in both, too.

average: deferral: 19% [8 – 28%]
Monitorize of the plasmapheresis donors of Whole blood donation's attitude

Issued Certificate about the Whole blood donation
(the plasmadonors have visited the HNBTS to give blood)

Whole blood donation in the plasmapheresis centres
(mobile site, team is belong to the HNBTS)
31,177 Donors: compliance of different type of donation 2017.

- Plasmapheresis & Whole Blood Donation: 10,245; 33%
- Plasmapheresis & No Whole Blood Donation: 20,932; 67%
No Whole Blood donation and different plasma donation attitude in 2017.

No Whole Blood donation N = 10 245 donor
- 1 plasmapheresis
- More plasmapheresis

7 648; 75%

2 597; 25%
Plasmapheresis & Whole Blood Donor
N = 20,932 in 2017.
Results

Improved communication among plasma centres and blood supply has begun, which will be provided with an IT support (unique donor -with cross reference register) in the close future.

The register improves both donors and patients safety.

HNBTs has got some new mobile (fix) collection places with more donations.

The plasmapheresis donors have collected information about the whole blood donation and labile blood products.
Conclusion

The advantage of the government decree to find a new donor population who will be involved in the whole blood donation management, too.

To evaluate the attitude of whole blood donation we need further study and to find the personal contact with these people.

Whole blood donation rate in the plasmapheresis donors were higher in 2018 than 2017.
Thank you very much for your attention
Italian regulation on plasma self-sufficiency programme

Giancarlo Maria Liumbruno (MD)
Director general
Italian National Blood Centre
Rome, Italy

Strasbourg, January 29, 2018
Disclosure

I hereby declare that I have neither financial nor non-financial relationships related to any of the products or services described, reviewed, evaluated or compared in this presentation.
Agenda

• Founding principles and main figures

• Italy’s self-sufficiency

• The Plasma and Plasma-Derived Medicinal Products National Plan 2016 - 2020
**Healthcare governance in Italy**

**Federalist framework since 2001**

**Delivering healthcare (HC) is by law delegated to the 21 Regions**

6 Autonomous Regions and Provinces (with additional autonomy/privileges):
- Aosta Valley
- Friuli-Venezia Giulia
- AP Trento
- AP Bolzano
- Sicily
- Sardinia

**Ministry of Health**

Responsible for:
- general healthcare legislation
- transposing EU provisions
- defining “basic healthcare levels” (BHCL)
- controlling BHCL application in the regions
- controlling regional budget balance
- general public health regulation

Any law / regulation must be preliminarily formally “shared” with Regions (State-Regions agreements)

Ministry of Economy strongly conditions the HC national budget (114.5 billion € in 2018; ≈ 6.4% of GNP)
Italy’s Blood System: founding principles

Voluntary, periodic, responsible, anonymous and not-remunerated donation of blood

Blood activities can be performed only by public blood transfusion organizations (qualified blood donor Associations specifically licensed and accredited)

Civic & social function and strategic role of the Donor Federations and Associations institutionally recognised

Donor Federations and Associations participate in the institutional scheme of the national and regional blood network

BEs (and HBBs) are exclusively public and hospital-based

Human blood is not a source of profit

The transfusion process is subject to specific accreditation that complies with European regulations

Transfusion medicine activities as well as blood donation promotion & development are recognised as “basic healthcare services”

The transfusion process is unitary and “indivisible”

to be delivered equitably, impartially and free of charge to any citizen needing them
Italy’s Blood System: strategic goals
Law 219 of 21st October 2005

- **Self-sufficiency** of blood and blood products, including plasma-derived medicinal products (PDMPs), is a national supra-regional strategic goal, i.e. independent of the regionalised organization of health-care delivery.
- **Promotion and continuous development** of voluntary non-remunerated (VNR), regular blood donation, and VNR donor retention.
- High **quality and safety** of blood components, transfusion medicine activities and PDMPs.
- **Compliance with European regulatory provisions** on blood and blood products (Italy has transposed and fully applies all the pertinent EU directives).
- **Appropriate management and clinical utilisation** of blood resources [including PDMPs and patient blood management (PBM) programmes)].
- Continuous development of transfusion medicine, aligned with scientific progress.
- Blood system’s accountability, effectiveness and sustainability.
Blood components collected in 2017

- 3,006,726 donations
  49.6 per 1,000 pop
- 2,579,438 WB donations
  85.8% of total donations
  42.6 per 1,000 pop
- 427,288 apheresis
  (348,486 plasmapheresis)
  14.2% of total donations
  5.6 per 1,000 pop

1.8 WB donations/donor/year
2.1 plasma donations/donor/year

Blood components transfused in 2017

- 2,960,643 units
  48.8 per 1,000 pop
- 2,457,300 units of RBCs
  40.6 per 1,000 pop
  (98.8% leucodepleted)
- 218,937 units of platelets*
  3.6 per 1,000 pop
  (25.2% apheresis)
- 284,406 units of plasma**
  4.7 per 1,000 pop
  (of which 119,404 virus-inactivated plasma)

8,111 blood components transfused per day

1 donation every 10 seconds guarantees transfusion therapy for 1,806 patients a day

* Adult therapeutic dose; ** apheresis + WB
Agenda

• Founding principles and main figures

• **Italy’s self-sufficiency**

• The Plasma and Plasma-Derived Medicinal Products National Plan 2016 - 2020
The annual national self-sufficiency programme

Self-sufficiency of blood and blood products, including PDMPs, is a national supra-regional strategic goal, i.e. independent of the regionalised organization of health-care delivery.

Since 2008, 10 annual national self-sufficiency programmes have been published and became law.

Every year, the Minister of Health, on the basis of the indications provided by the National Blood Center in accordance with Regions, annually defines the national self-sufficiency programme, which identifies:

- the historical consumption,
- the real needs,
- the production levels required,
- the resources,
- the criteria for financing the system,
- the organisational methods and the tariff references for the compensation between the regions,
- the levels of import and export that may be needed.
National self-sufficiency of PDMPs

• “[...] to provide patients, in a systematic and sustainable way, with the prompt and continuous availability of a defined set of PDMPs with the highest level of quality and safety and in compliance with the existing regulatory framework, which meets appropriate clinical needs through the national collection of plasma based on VNRDs with the contribution of PDMPs shares acquired on the market.”

Plasma for fractionation (PfF) 2000-2017

Source: Adapted by the Italian National Blood Centre on data from Fractionation industries, January 2019
Italy’s self-sufficiency in 2017

- **ALBUMIN**: 70%
- **ANTITHROMBIN**: 76%
- **IV IMMUNOGLOBULIN**: 73%
- **FACTOR VIII**: 71%, 55%
- **S/D-TREATED PLASMA**: 82%
- **FACTOR IX**: 83%
- **PCCs3**: 96%

Agenda

• Founding principles and main figures

• Italy’s self-sufficiency

• The Plasma and Plasma-Derived Medicinal Products National Plan 2016 - 2020
Main goals

• the adoption of measures for promoting the **appropriate use of PDMPs**;

• the **promotion of the collection**, with particular regard to the Regions that have low plasma donation levels;

• the **improvement of the efficiency** of the plasma collection system, with particular regard to plasmapheresis procedures.
Promoting the appropriate use of PDMPs

Regional demand for

- Albumin shall not exceed 400 grams per 1,000 pop ..... 
- AT shall not exceed 1 IU *per capita* ..... 
- Polyvalent immunoglobulins shall not exceed 110 grams per 1,000 pop .... 
- FFP shall not exceed 1,600 mLs per 1,000 pop .... 

- .... in the absence of documented epidemiological and clinical peculiarities
Main goals

- the adoption of measures for promoting the appropriate use of PDMPs;
- the promotion of the collection, with particular regard to the Regions that have low plasma donation levels;
- the improvement of the efficiency of the plasma collection system, with particular regard to plasmapheresis procedures.
PfF 2015

Adapted by the Italian National Blood Centre on data provided by Kedrion. June 2016.
PfF 2018

PfF 2000-2018 and PNP 2020 target

- Adapted by the Italian National Blood Centre on data from Fractionation Industries. January 2019

2.1 plasma donations/donor/year
12 litres/year
24 donations/year
600-700 mL volume

- 839,535
- 860,733
2020 target
Plasma and PDMP National Plan

Main goals

• the adoption of measures for promoting the appropriate use of PDMPs;
• the promotion of the collection, with particular regard to the Regions that have low plasma donation levels;
• the improvement of the efficiency of the plasma collection system with particular regard to plasmapheresis procedures.
Improvement of the efficiency of plasma collection, with particular regard to plasmapheresis procedures
Actions aimed at improving the efficiency and sustainability of plasma collection

- **Increasing procedures per apheresis machine**
  - **600 procedures** per machine per year (Regional average)
  - Minimum: **250 procedures** per machine per year

- **New partnerships and agreements with voluntary blood donor Associations and Federations**

- **Increasing the accessibility** to BEs and blood collection sites

- **Increasing volumes collected** through apheresis procedures
  (min 600 – max 700 mL: +18%; up to 12 L/year and 24 plasma donation/year)

- **Reducing discarded plasma units** (< 2% of collected units)
Conclusions 1

• In Italy, Plasma and PDMPs are part of a **specific national regulation** which defines **levels of collection** for each Region and **appropriate levels of demand** for PDMPs, aligned with expected scenarios, and includes several areas of improvement and measures to intensify plasmapheresis.

• **VNRDs and donor Associations** as part of the Italian blood and plasma system, which is entirely public, **are able to provide** as much plasma as needed to obtain significant levels of PDMP self-sufficiency despite “relatively low” levels of plasma donation.

• **EU legislation is an opportunity** for strategic independence of PfF [VNRDs, blood donor health and safety]
Conclusions 2

• An EU Plasma and PDMP self-sufficiency plan based on VNRDs could integrate single Member State plans and include shared (and more easily adopted) «Proposals for a way forward to intensify plasmapheresis»

• PDMP self-sufficiency based on VNRDs could/should be a common European strategic objective

• The main obstacle to the independence of PfF in Europe is possibly the lack of awareness that:
  • Plasma itself is a strategic resource as “raw material” for the production of life-saving medicinal products
  • Currently, the global plasma and PDMP-market depends almost entirely on plasma collected in the USA
  • PDMP self-sufficiency based on VNRD is possible (Yes, we can!)
Thanks for your attention!
PLASMA COLLECTION in the CZECH REPUBLIC

P. Turek, V. Řeháček
CZ
Blood Transfusion Service in the Czech Rep.

population: 10.6 mil.      country size: 79 thds sqkm
hospitals: 188

- 68 blood-establishments (BE), hospital-based, merged with BB (incl. 52 full-scope BEs + 16 collection centers)
- 62 indep. blood banks (BB)
- 19 independent (commercial) plasma-collection centers (plasma for fractionation only)
Rules and regulations (1)

- Whole blood donations: men 5 / year; women 4/y min. interval 8 weeks

- Plasma donations:
  - min. interval 2 weeks
    (since 2011, earlier min. 7 days)
  - max. volume per donation 650 ml of plasma
    (if i.v. volume is not supplemented)
  - max. volume 25 litres/year (excl. anticoagulans)

- WB => plasma interval min. 4 weeks
  (plasma => WB min. 2 days)
Rules and regulations (2)

Voluntary nonremonerated donation:
(nearly all donations in hospital-based BTS)
- reimbursement of travel expenses and direct costs
- small refreshment
- possible tax deduction

Compensated donation:
(vast majority of plasma collections in plasma-centres)
- compensation of time lost, inconvenience, travel expenses ...
  (max. amount regulated by law = cca 25 Euros / donation)
- small refreshment
Blood donors regular / first time (in thds.)

- **First-time donors**
  - 2007: 20
  - 2009: 60
  - 2011: 50
  - 2013: 50
  - 2015: 40
  - 2017: 40

- **Regular donors**
  - 2007: 300
  - 2009: 350
  - 2011: 350
  - 2013: 350
  - 2015: 350
  - 2017: 350

- **Legend**
  - **Hospital based BE’s**
  - **PLMF centres**
Blood / plasma donations (in thds.)
Age of donors in hospital-based BTS comparison 2008 / 2016

No. and percentage of young first-time-donor decreased

mean age of repeat / regular donors increased

(based on study in representative sample of hospital based BTS, Turek el al., in press)

NB: data from plasma centers in CZ are not available
Infection rate in blood donors (hospital based BTS versus plasma-centers)

number of positive donations / 100 000 donations
Plasma production / usage (litres in thds.)

Clinical use: FFP+source  Frakció: FFP  Frakció: source from BE´s  Frakció: source from PLMF centers
Distribution of CZ plasma for fractionation in 2017:

- WB derived plasma: 72,3 thds. litres
- source plasma from BE´s: 143,4 thds. litres
- source from plasma-centers: 429,0 thds. litres
- Total: 644,7 thds. litres

Example:

- WB derived plasma: 6,9 l / 1000 inhab.
- source plasma from BE´s: 13,4 l / 1000 inhab.
- source from plasma-centers: 40,8 l / 1000 inhab.
- Total: 61,1 l / 1000 inhab
Distribution of plasma products in CZ

F VIII (I.U. per capita)

immunoglobulins (g/1000 inhab.)

albumin (g/1000 inhab.)

fibrinogen (g/1000 inhab.)
Need of plasma for fractionation in CZ

in 2017:

• albumin 160 g / 1000 inhab.
• FVIII (plasma derived) 2,8 KIU / 1000 inhab.
• immunoglobulins 42 g / 1000 inhab.

eg. as „plasma needed“:

• albumin (yield 20-25 g/l) < 9 litres / 1000 inhab.
• FVIII (yield 180-200 IU/l) <16 litres / 1000 inhab.
• immunoglobulins (yield 3-5 g/l) <14 litres / 1000 inhab.

CAVE: what is necessary and medically justifiable need of plasma products?
Czech experience ....

• coexistence of „standard“ blood transfusion service and commercial plasma-collection centers didn´t harm national self-sufficiency in blood components during last 10 years

• over 60 liters of plasma / 1000 inhab. can be collected respecting CoE limits for donation frequency / volume

• over 20 liters of plasma for fractionation / 1000 inhab. are collected from voluntary non-remunerated donors (plus 5 litres / 1000 inhab. for clinical use)
CZ questions ....

- does plasma centers compete with hospital-based BTS in donor recruitment? Is the co-existence long term sustainable? Are there any limits?
- what is the effect of compensation on donor / plasma safety?
- is an intensive regimen of plasma collection safe for everybody?
- what instruments should the Government keep for regulation of plasma donation in case of shortage in blood components?
Suggestions / recommendations

- national self-sufficiency in production of plasma for fractionation should be a goal
- donor health should be of major concern
  (increasing of CoE limits for plasma donation is not necessary)
- balance between WB and plasma donations should be set / controlled according to national needs
- level of „compensation“ should be limited / regulated
- cooperation of blood transfusion centers and plasma-collection centers is advisable  (for example, sharing of registry of donors excluded for positivity of infectious markers …)
Thank You for Your attention
The ruling in the Medisanus case

Irena Razboršek
Blood Transfusion Centre of Slovenia
Symposium on Plasma Supply Management
29-30 January 2019
Description of the case

• On January 2015 Murska Sobota general hospital launched a tendering procedure for the supply of medicinal products:
  • Human blood albumin 200 mg/ml infusion solution, obtained from Slovenian plasma
  • Human immunoglobulin for intravenous administration, 50 mg/ml or 100 mg/ml, obtained from Slovenian plasma
Description of the case

• On 25 February 2015 Medisanus (company having its seat in Ljubljana, Slovenia) requested the contracting authority to review the tender specification

• On 23 March 2015 the contracting authority rejected the request (the specification are in accordance with national law)
Description of the case

• Medisanus submitted a request for revision to the National Commission for the review of awards of public procurement procedures (Državna revizijska komisija za revizijo postopkov oddaje javnih naročil)

• The National Commission had doubts (it might give rise to a breach of principles of equal treatment)

- and refer the question to the Court for a preliminary ruling
Case C-296/15

• Request to the Court:
  • Interpretation of Article 2 and Article 32(2) and (8) of Directive 2004/18
  • Article 83 of Directive 2001/83
  • Article 4(2) of Directive 2002/98/EC
  • Article 18 TFEU

• The request was received to the Court on June 2015
• Opinion of Advocate General 1 December 2016
• Judgment of the Court (Third Chamber) 8 June 2017
The Court (Third Chamber) rules:

• Article 2 and Article 23(2) and (8) of Directive 2004/18/EC of the European Parliament and of the Council of 31 March 2004 on the coordination of procedures for the award of public works contracts, public supply contracts and public service contracts, and Article 34 TFEU read in conjunction with Article 36 TFEU, must be interpreted as precluding a clause in the tender specifications for a public contract which, in accordance with the law of the Member State to which the contracting authority belongs, requires medicinal products derived from plasma, which are the subject matter of the public procurement at issue, to be obtained from plasma collected in that Member State.
Rules of EU law concerning human blood

• According to recitals 2, 4, 23 and 32 of Directive 2002/98, which governs various operations in relation to human blood:

• ‘(2)’ The availability of blood and blood components used for therapeutic purposes is dependent largely on Community citizens who are prepared to donate

• (4) ... Furthermore, Member States should take measures to promote Community self-sufficiency in human blood or blood components and to encourage voluntary unpaid donations of blood and blood components
Article 110 of Directive 2001/83

• ‘Member States shall take the necessary measures to promote Community self-sufficiency in human blood or human plasma. For this purpose, they shall encourage the voluntary unpaid donation of blood and plasma and shall take the necessary measures to develop the production and use of products derived from human blood or human plasma coming from voluntary unpaid donations. They shall notify the Commission of such measures.
Article 6(71) of the Zakon o zdravilih (Law on medicinal products) (Uradni list RS, No 17/14) provides:

- The **priority supply of medicinal products** industrially manufactured from Slovenian plasma (that is to say, from frozen fresh plasma for processing, collected in the Republic of Slovenia) constitutes a principle whereby medicinal products obtained from foreign plasma which originate in the European Union are to be supplied on the basis of a marketing authorisation, in the event that medicinal products prepared from Slovenian plasma fail to cover the total demand for such products in the Republic of Slovenia, except where the introduction or importation of a specific medicinal product obtained from foreign plasma is justified on scientific or strategic grounds, as defined by the Strateški svet za zdravila [(Strategic Council for pharmaceutical products, Slovenia)] and by the Strokovni svet za preskrbo s krvjo in z zdravili iz plazme [(Scientific Council for the supply of blood and medicinal products obtained from plasma, Slovenia)].
The Law on the supply of blood
Article 2 (Uradni list RS, No 104/06) provides as follows:

• 1. The supply of blood under this Law forms part of transfusion activities, which include planning, collection, processing, testing, storage, distribution and medical treatment as well as the regular and sufficient supply of blood and blood products to the population and the marketing of such products.

• 2. The activities referred to in the previous paragraph shall be carried out in accordance with the principles of national self-sufficiency and of voluntary unpaid blood donation, in order to guarantee a sufficient number of donors and the safety of blood transfusions.
In Article 3(11), (12), (13), (18) and (27) of that law, the following terms are defined as follows:

- ‘blood’ is defined as ‘whole human blood’;
- ‘blood component’ is defined as ‘an active component of blood (... plasma), which may be prepared from blood by various methods’;
- ‘blood product’ is defined as ‘any therapeutic product (component or medicinal product) which is derived from human blood or human plasma’;
- ‘self-sufficiency’ is defined as ‘the principle relating to the supply of blood and blood products under which the State is to meet its demand for blood and blood products using its own resources’; and
- ‘blood-based medicinal product’ is defined as ‘any medicinal product obtained from human blood or human plasma’.
Article 5(1) of that law

• The activity of collecting and testing blood and blood components, whatever their intended purpose, and their processing, storage and distribution, when intended for transfusion, **shall constitute a public service**. The service shall be performed by the institute of transfusion or by the transfusion centre designated and licensed by the Agency.
Article 10(1) and (2) of that law

• determines the function of the Blood Transfusion Centre (‘the Institute’) in the following terms:

• 1. The [Institute] is ... responsible at national level for the supply of blood and blood products to professional bodies, and for the integration of transfusion medicine in hospital practice.

• 2. The [Institute] shall coordinate all activities concerning donor selection, the collection, testing, processing, storage and distribution of blood and blood products, the clinical use of blood ...’
Responsibility ZTM in medicinal product

• Only the surplus amounts of blood collected are intended to be processed into medicinal products such as human albumin or human immunoglobulin, which form the subject matter of the call for tenders at issue in the main proceedings.

• SLO does not itself process the blood collected in Slovenian territory into medicinal products, but sends that blood to a private operator which manufacturers the medicinal products by means of an industrial process. The ZTM selects that operator within the framework of an open procurement procedure in accordance with Directive 2004/18.
• The medicinal products thus obtained are intended exclusively for the Slovenian market. The ZTM distributes those medicinal products to other public health services in Slovenia, and in particular to the hospitals. By way of consideration, the ZTM receives only the costs of manufacturing.

• Furthermore, it is only if and in so far as the quantity of medicinal products manufactured on the basis of Slovenian plasma is not sufficient to satisfy the needs of the Slovenian population that medicinal products manufactured on the basis of foreign plasma are bought, within the framework of an open public procurement procedure in accordance with Directive 2004/18.
History of the Supply medicinal product from plasma

- Until 1990 albumin and imunoglobin from SLO plasma was produced in Zagreb
- Patient with hemophilia were treated with FFP, cryo and rarely with imported coagulation factors (HIV!)
- Due to the risk of transmission of viral infections with blood products, the requirements regarding the safety and quality of medicines from the blood became stricter
- Government launched Memorandum on the Safety of Hemophilia Treatment
- 1991 selection of a new contractor
Article 28 (export of blood and blood component)

- The minister of health may allow the export of blood and blood components upon humanitarian and professional assistance...
After judgment of the Court

- In Slovenia, we advocate very strongly that national efforts towards self sufficiency is a way to self sufficiency in Community. Blood, blood components (plasma included) are substances of human origin.

- All donations should be based on voluntary, unpaid donations and a high protection of blood donors health should be as important as high protection of patients health.

- In Slovenia app. 60 – 65 % albumin and immunoglobulin is covered with medicinal product produced from Slovenian plasma.

- According to the Decision of the Ministry of Health those products are sold to hospitals in proportion to their consumption
• Commission has pointed out in its written observations ......they prefer selling medicinal products derived from plasma in countries that can pay a higher price or buy them on a larger scale. Smaller States are thus facing a significantly higher price for medicinal products derived from plasma.

• The Slovenian Law of drugs is in a process of change.
Belgium
Recent program to increase plasmapheresis for PDMP

Philippe Vandekerckhove, MD, PhD
Belgian Red Cross
Facts & Figures Belgium Blood Banking system

• 11.5 million inhabitants
• Separate legislation
  • Labile blood products
  • Stable blood products
• Universal VNRD (whole blood, plasma, platelets)
• Responsibilities
  • Federal Ministry of Health
  • Competent authority: Federal Agency for health products
4 Licensed Blood Establishments

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<th>Blood institution</th>
<th>% RBC</th>
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<td>Flanders</td>
<td>62</td>
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<tr>
<td>Belgian Red Cross-Flanders</td>
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<tr>
<td>Frenchspeaking Belgium</td>
<td>Croix Rouge de Belgique-Comm Francophone</td>
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<td>CHU Mont-Godinnee</td>
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Initiative Belgian Government: budget

LITERS

- total (budget)
- PF (budget)

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<th>PF (budget)</th>
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Budget projections for the years 2017 to 2021.
Initiative Belgian Government: realisation

LITERS

- total (budget)
- total (realised)
- PF (budget)
- PF (realised)

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<td>2021</td>
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Budget increase from 5% to 32%
Historical Overview Plasmapheresis *(Flanders, Belgium)*

- **Donations**
- **LITER**
- **Donations (Budgeted)**
- **LITER (Budgeted)**

Graph showing donations and liter over the years from 1972 to 2020.
Historical Overview Plasmapheresis *(Flanders, Belgium)*
Analysis

It is not enough to do your best: you must know what to do, and then do your best.

Edwards Deming (1900-1993)
Donations: plasma vs whole blood *(Flanders, Belgium)*

![Graph showing blood donations and plasma donations from 2009 to 2021.](image)
Suggestions & Conclusions