Introduction

- House keeping information
- EDQM / EU Commission, not to be confused
- Regulatory framework

Council of Europe (SXB)

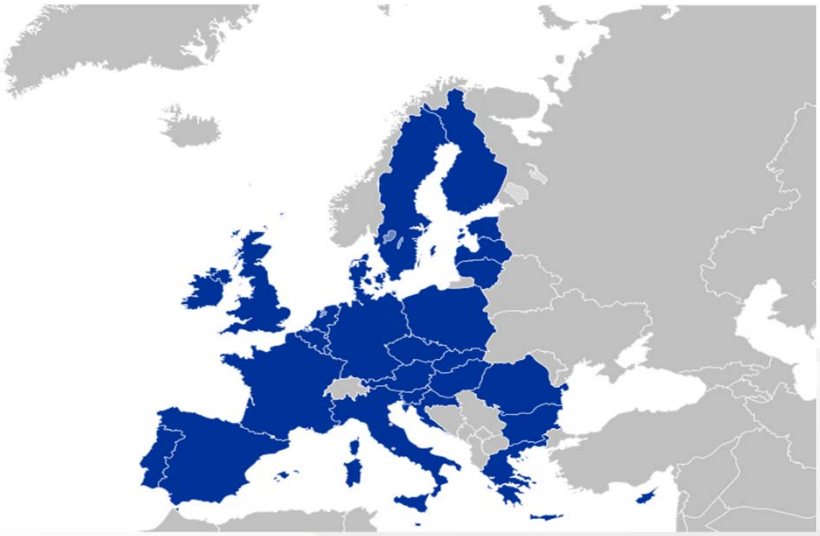
- 47 Member States
- 12 countries in 1949
- to promote democracy, human rights, rule of law
- Conventions, CM res/rec
- European Pharmacopoeia in 1964 (38 MS & EU)
  - Public health by common quality standards

European Union (BRU)

- 28 Member States
- 6 countries in 1951,
- European Coal and Steel Community, EEC, EU
- Treaties (Rome 1957, Maastricht 1993, ...)
- Single market, free movement: Goods, incl. Pharmaceuticals
- Minimum safety and quality requirements: blood & blood components & pharmaceuticals)

Council of Europe (SXB)
820 Million of Europeans

European Union (BRU)
500 Million of Europeans



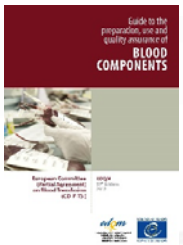
Democracy – Human Rights – Rule of Law

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



Components + Plasma

Testing | Testing

WB-collection | Plasma-pheresis

Donor

Patient

Fractionation → PDMP

Pharmaceutical Legislation

EU GMP
Annex 14, rev 1

Dir 2001/83/EC
as amended

European Pharmacopoeia

Patient

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, fo
  groups, …)
- Bilateral Meetings
- Multi-lateral Meetings EU-national-stakeholders. …

COM Staff Working Document (1H 2019)

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)*

https://ec.europa.eu/health/blood_tissues_organs/policy/evaluation_en

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"

Response	Number of Responders
Compensation for time and travel	3
Fixed amount per donation	7
Token or Gift	3
Reward Program	1
None	10

Guide standards for plasmapheresis per donor and year

- max 750 mL, excl. anti-coagulants, per donation
- max 33 plasmapheresis donations
- max 25 L plasma

Practices compared to Guide standards	BE: lower/aligned	BE: higher
Collection volume	15	9
Donations	15	8
annual volume	17	7

Practice versus standards: donations per donor LFY

CoE Guide standard: max 33 donations per year

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

Methods to decide collection volume

Guide standard:
total blood volume must be estimated

Method	BE	Collections
• Bodyweight (with max volume) (data by 10 BE)	11	783 306
• Gender, weight and height	6	1 306 789
• Algorithm in equipment	2	42 557
• Standard volume	2	15 298
• XXX protocol	1	703 857
• Not specified	2	36 533

Medical assessment

23 BE	At first donation	At repeat donations	
		Everytime	Other frequency
DHQ+interview	23	18	
Weight	19	16	
Height	5	2	
Hb ¤	22	18	
Blood pressure/ pulse rate	21 /19	17	
Body temperature	7	7	
Physical exam	8		1

¤ 13 require a higher level of Hb than Guide standard for plasmapheresis

Screening for infectious markers

21 BE	At first donation	At repeat donations
Standard HIV and HCV serology HBsag	20	20
HIV/ HBV/ HCV NAT	16/14/15	16/14/15
Syphilis ab	10	10
Other tests	7	7

Standards: total protein, electrophoresis (SPE) or albumin and IgG before start and at least annually. ABO RhD may be waived

22 BE	At first donation	At repeat donations	
		Every time	Other frequency, at least annually
IgG, some incl. IgA and/or IgM	20	2	10
Total protein	17	5	15 (2 also do SPE)
Albumin	4		6
Full blood count	15	9	6
ABO/RhD	19	12	1
RBC ab screening	20	7	6 (4 only if possible immunisation)

Practices to capture and report donor adverse events

Guide standard: report all adverse events

Adverse events captured	All	Selected
BE	20	4
Reporting system used		
Electronic system	16	2
Other system	3	2
Not specified	1	

Adverse event surveyed

rate/10 000 collections requested

Type of adverse event	Respondents
• Overall adverse event rate	18
• Acute vasavagal reaction, no loss of consciousness	18
• Acute vasovagal reaction, loss of consciousness	17
• Delayed vasovagal reaction, no loss of consciousness	17
• Delayed vasovagal reaction, loss of consciousness	16
• Citrate reaction	16
• Haemolysis	19
• Extravasation	12

Varying number of respondents negated various types of events

Apheresis equipment used LFY

Equipment	BE	Collections
• PCS2, MCS+, ns	13	750 258
• Mixed	5	927 174
• Trima	1	573 624
• Aurora	1	6 328
• Not indicated	3	643 756

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

PDMPs

Voice of the patients:

patient perspectives & views situation & future needs in PDMPs

Frank Willersinn, MD
alpha1plus@yahoo.be

PLUS
Platform of Plasma Protein Users

Conflicts of interest
> none

patient representatives

&

IPFA
EBA
EPA
PPTA
IFBDO
…

PDMPs

Platform of Plasma Protein Users

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 availibility
5. Conclusion / last ideas

About the patient

- Life threatening medication

- Avoiding crisis or situations of emergency

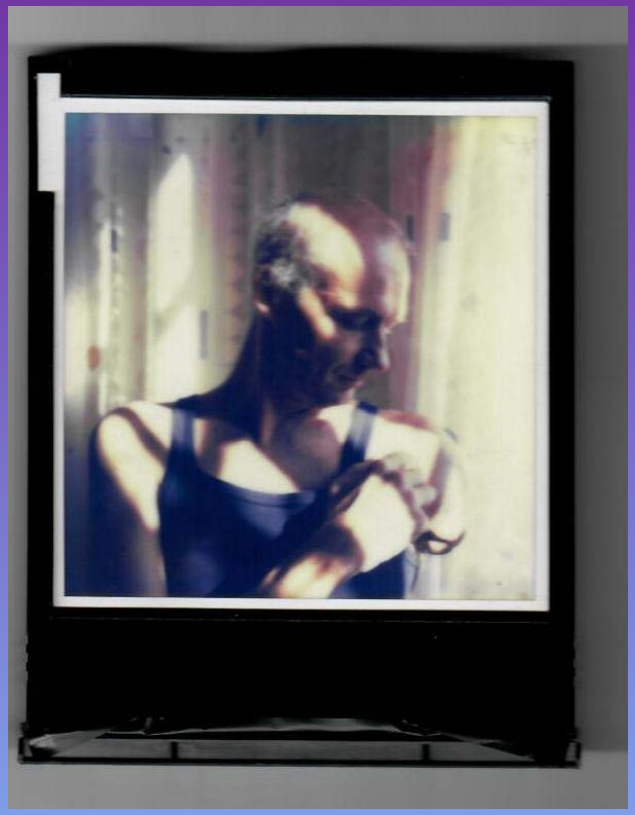
- Quality of life & social welfare
  - pain
  - security
  - social life & integration
  - well beiing

THE PATIERNT DOES NOT CARE WHERE HIS PRODUCT COMES FROM – BUT HE IS GRATEFUL!

Platform of Plasma Protein Users

disease: Alpha-1 antitrypsin deficiency

Genetic
Rare disease
Liver (newborns) & lung (emphysema COPD)
oxygen
Lung transplant



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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

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 unacceptabel

GPS - Guillain-Barré syndrome

CIDP - Chron. Inflammat. 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

	AATD	Hemo + RBD	PID	GPS	C1 IE	Alb
						More indications
Shortcuts	+		+	?	some	
Underdiagnosed		VW factor			+/-	
Needs next 5 years	++	+/-	+++	+	same	+

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

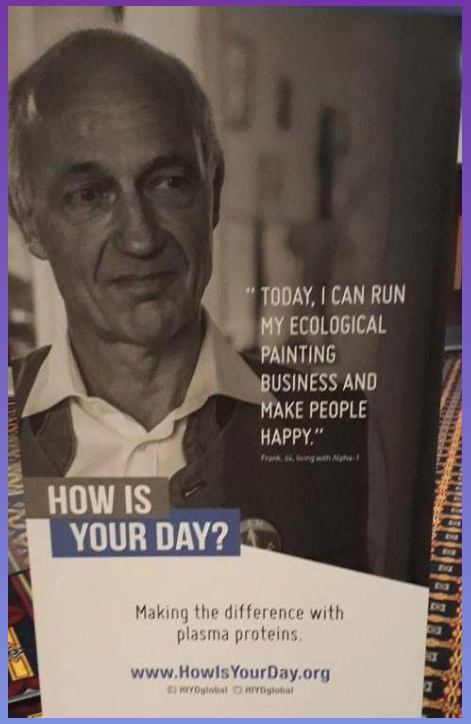
4. proposals to increase availibility

Platform of Plasma Protein Users

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

>> Make it known !

Métro advertising, Brussels, July 2018



Platform of Plasma Protein Users

to create awareness: an issue of communication

sensitization

Explain –> convincing –> motivation

donation

Education :

health is a major issue in wellbeiing

sensitize	in universities , schools (get nurses to schools as health educators)
Create awareness	about Rare Diseases about the need for plasma & possibilities to donate
Create tools to communicate	to patients in an understandable language to the medical community in an easy way

Platform of Plasma Protein Users

European Commission - Statement

International Blood Donor Day: Statement by Commissioner Vytenis Andriukaitis

Brussels, 14 June 2018

On 2018 World Blood Donor Day, let us remember that blood is the lifeline that connects us a we all have a pivotal role to play in donating blood to help save lives. In particular, I would lik invite young people to come forward, to ensure that our blood banks do not diminish and are constantly replenished.

Blood transfusions are a vital medical intervention used worldwide to treat a wide variety of both in emergency and non-emergency settings. The majority of these disorders can be life threatening without a timely blood transfusion, which is why the immediate availability of s lood is paramount. As a former cardiac surgeon, I know how true this is.

o encourage blood transfusions and avoid related complications, including the transmissi seases from donor to recipient the EU has laid out directives that set out safety standar llection. Moreover, the European Commission is currently carrying out the first formal s legislation since its adoption in 2002. The evaluation is taking an in-depth look to se islation has achieved its objectives and if it is still fit for purpose. As there have been ntific, societal and epidemiological changes since 2002, I believe that our citizens d efit from the latest developments in health and safety.

European Commission also actively supports EU countries, through the Public Hea ntinuously improve blood donation and blood supply programmes, appropriate c ous resource and effective oversight procedures for ensuring safety and quality.

International Blood & Plasma Day: June 14th

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Create new values:

Donation

can be a social value of identity & recognition

Platform of Plasma Protein Users

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
- …

+ Partnerships

« which ‘ideas’ will make people make donate in 2025 ? »

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EP, January 22nd 2019

…when marketing meets communication:
Netherlands 2019: donor recruitment for rare blood groups

Also:

> Promote plasmapheresis programms where feasible

> Plasma from hemochromatosis patients

> honor the donor: new definition of Compensation

> get better National plasma donator database

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Management for supply and availability:
Flexibility of firms, of countries

~~shortages~~

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

Pharmacovigilance:
Data collection of side effects,
patient reported outcomes

Who is motivated today ?

friend

aunt

colleague

neighbour

Cooperation

Work out more altruisme

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Interaction

Educate !

Compromises

- lexibility

synergy

The patient needs you !

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PLATFORM OF PLASMA PROTEIN USERS

Platform of Plasma Protein Users (PLUS)
STAKEHOLDERS CONSENSUS CONFERENCE 2019
Intercontinental Hotel, Estoril
PORTUGAL
24-25 January 2019

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PROTEIN USERS

PLUS Consensus Principles on Strategies
to encourage Blood and Plasma Donations in Europe

PLUS
PLATFORM OF PLASMA PROTEIN USERS

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).

Edit.resp. : Johan Prévot, PLUS, Av. Aida, Bloco 8, Esc. 821, 2765-187 Estoril, Portugal, johan@ipopi.org,

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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.

Estoril, January 25th 2019

*

Stakeholders endorsing:

- Alain Weill (World Federation of Hemophilia)
- Albert Farrugia (University of Western Australia)
- Bob Perry (International Plasma and Fractionation Association)
- Dominika Misztela (Plasma Protein Therapeutics Association)
- Frank Willersinn (Platform of Plasma Protein Users, Alpha 1 Global)
- Jan Bult (Plasma Protein Therapeutics Association)
- Johan Prevot (Platform of Plasma Protein Users, International Patient Organisation for Primary Immunodeficiency)
- Jose Drabwell (International Patient Organisation for Primary Immunodeficiency)
- Karl Petrovsky (Plasma Protein Therapeutics Association)
- Leire Solis (International Patient Organisation for Primary Immunodeficiency)
- Mark Brooker (World Federation of Hemophilia)
- Mark Skinner (American Plasma Users Coalition)
- Martin van Hagen (Rotterdam Erasmus Medical University Hospital, International Patient Organisation for Primary Immunodeficiency)
- Martine Pergent (International Patient Organisation for Primary Immunodeficiency, IRIS)
- Patricia Blomkwist (Guillain-Barré Syndrome/ Chronic Inflammatory Demyelinating Polyneuropathy, Multifocal Motor Neuropathy)
- Patrick Robert (Market Research Bureau)
- Paul Strengers (International Plasma and Fractionation Association)
- Saara Kiema (International Patient Organisation for Primary Immunodeficiency)
- Stephan Walsemann (European Plasma Alliance)

*

Edit.resp. : Johan Prévot, PLUS, Av. Aida, Bloco 8, Esc. 821, 2765-187 Estoril, Portugal, johan@ipopi.org.

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IPFA, embedded in community

international plasma and fractionation association

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**

DIRECTIVE 2002/98/EC OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL

of 27 January 2003

setting standards of quality and safety for the collection, testing, processing, storage and distribution of human blood and blood components and amending Directive 2001/83/EC

(6) The Commission's Communication of 21 December 1994 on Blood Safety and Self-sufficiency in the European Community identified the need for a blood strategy in order to reinforce confidence in the safety of the blood transfusion chain and promote Community self-sufficiency.

COMMUNICATION FROM THE COMMISSION ON

BLOOD SAFETY AND SELF-SUFFICIENCY IN THE EUROPEAN COMMUNITY

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.

Com (94) 652 final
Brussels
21-12-1994

This presentation

- European self-sufficiency of PDMPs
- Adequate collection of recovered / apheresis plasma

IPFA, embedded in community

international plasma and fractionation association

European self-sufficiency of PDMPs

The position of PDMPs in the health care' landschape

- 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

and

- 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.

WHO Expert group. Expert Consensus Statement on achieving self-sufficiency in safe blood and blood products, based on voluntary non-remunerated blood donation (VNRBD). Vox Sanguinis 2012, 103, 4: 337-342.

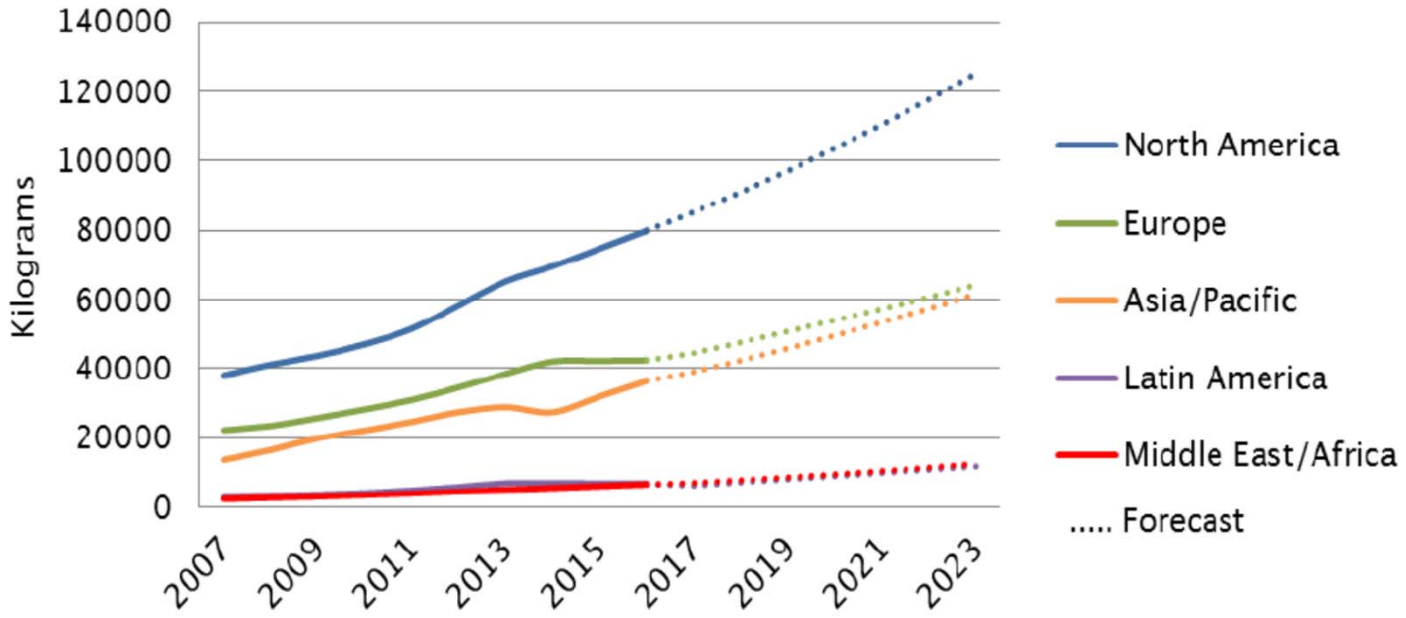
Challenges on self-sufficiency of PDMPs:

- 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) **?**

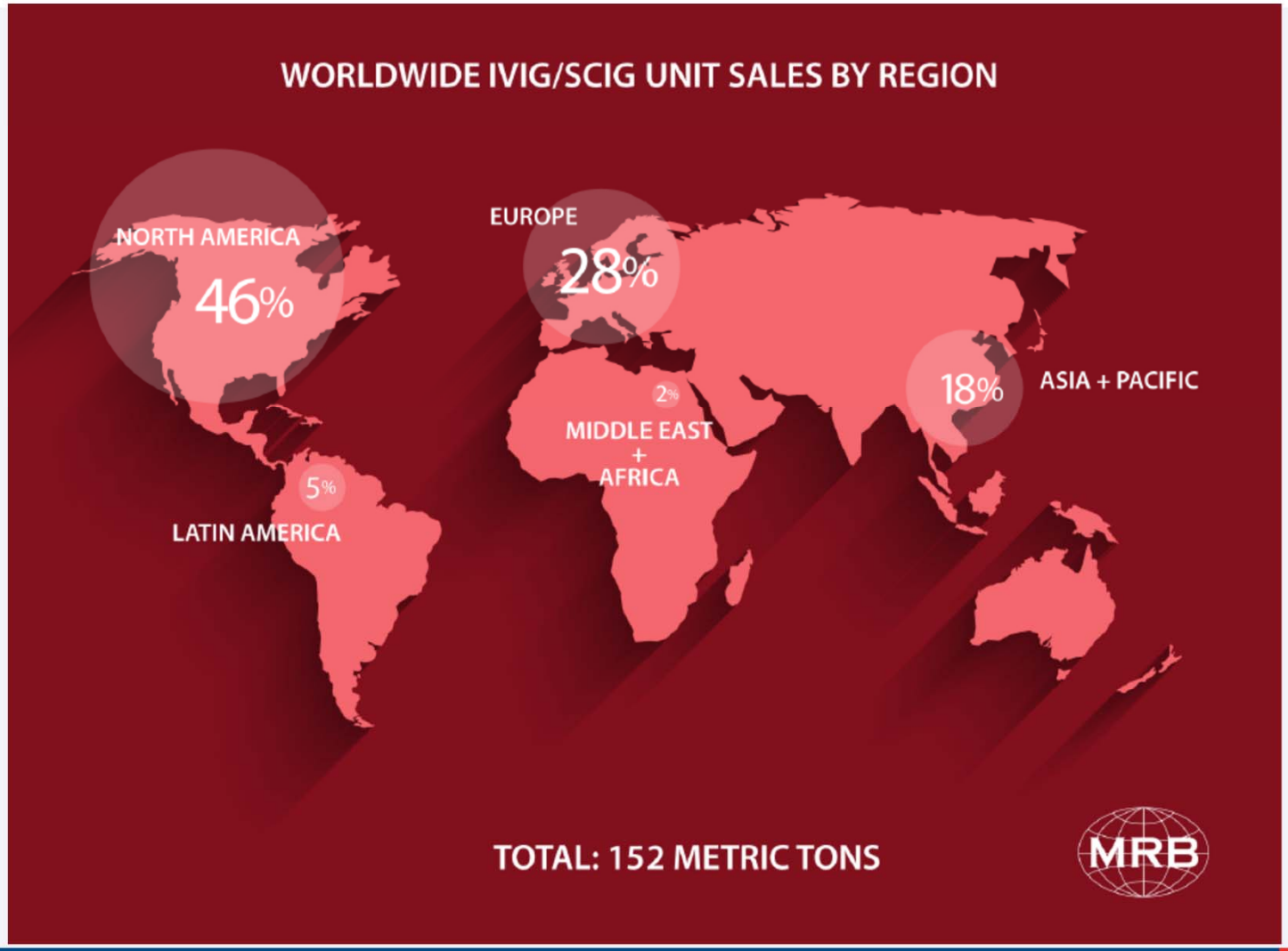
Global IgG demand – Actual and Projected

Figure 2.



Data from MRB (2015) Forecast of the Global Immunoglobulin Market (2014–2023).

Ref.: Protecting access to immune globulins for Canadians. Final report. May 2018.

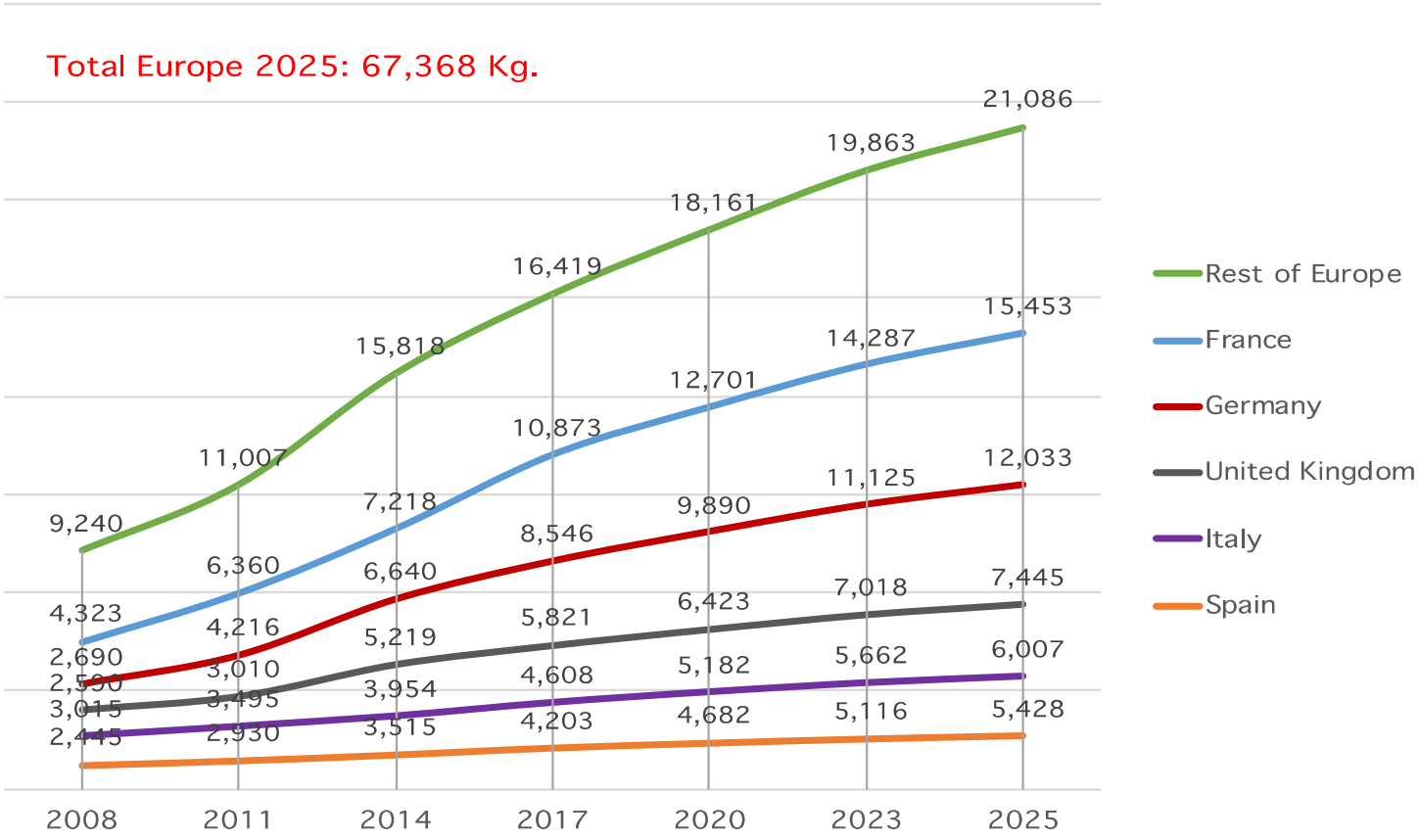


What is to be expected when Asia and Africa with their dense and increasing population become integral part of the
global market?

IPFA, embedded in community

international plasma and fractionation association

IVIG & SCIG CONSUMPTION BY COUNTRY IN EUROPE
2008 - 2025 - Kilograms



MRB

Ref. P. Robert, PLUS conference 2019, 24-01-2019

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.

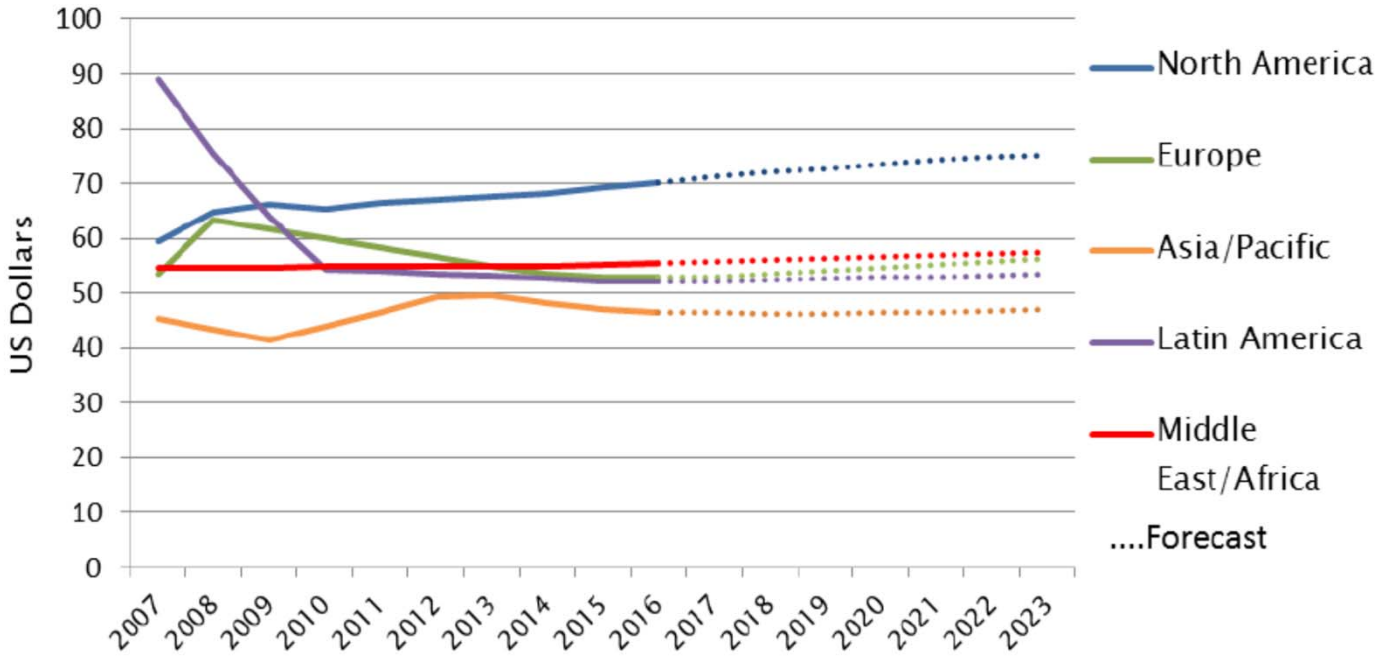
2018 Romania:

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)



Data from: MRB (2015) Forecast of the Global Immunoglobulin Market (2014–2023)

Ref.: Protecting access to immune globulins for Canadians. Final report. May 2018.

Aim: not self-sufficiency, but strategic independence

Strategic independence has the objective to create a balance against the current depedency 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]
- economic and political factors [America first. *Ref.: Lancet 2018, 392:447-450*]
- commercial consolidation
- changes in demand
- flow of medicines from low price to high price countries [Romania IgG crisis]


COMMENTARY

Plasma is a strategic resource

Paul F.W. Strengers[1,2] and Harvey G. Klein[3]

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)

	2017					
	IgG Consumption (Kilograms) (a)	Volume of Plasma Liters Needed - yield 4 grams/liter (b)	Volume of Plasma for fractionation available domestically			Shortfall of Plasma for fractionation (Liters) (b)-(e)
			Recovered (Liters) (c)	Apheresis (Liters) (d)	Total (Liters) (e)=(c)+(d)	
France	10,873	2,718	632	260	892	1,826
Germany	9,032	2,258	985	1,977	2,962	(704)
Italy	5,500	1,375	620	210	830	545
Spain	4,203	1,051	353	20	373	677
United Kingdom	5,821	1,455	-	-	-	1,455
Rest of Europe	15,041	3,760	1,516	2,193	3,710	51
Total Europe	50,470	12,618	4,107	4,660	8,767	3,851

	2025					
France	15,453	3,863	600	283	884	2,979
Germany	12,033	3,008	935	2,155	3,090	(82)
Italy	6,007	1,502	589	229	818	684
Spain	5,428	1,357	336	22	358	999
United Kingdom	7,445	1,861	-	-	-	1,861
Rest of Europe	21,086	5,272	1,592	2,390	3,983	1,289
Total Europe	67,453	16,863	4,053	5,080	9,132	7,731

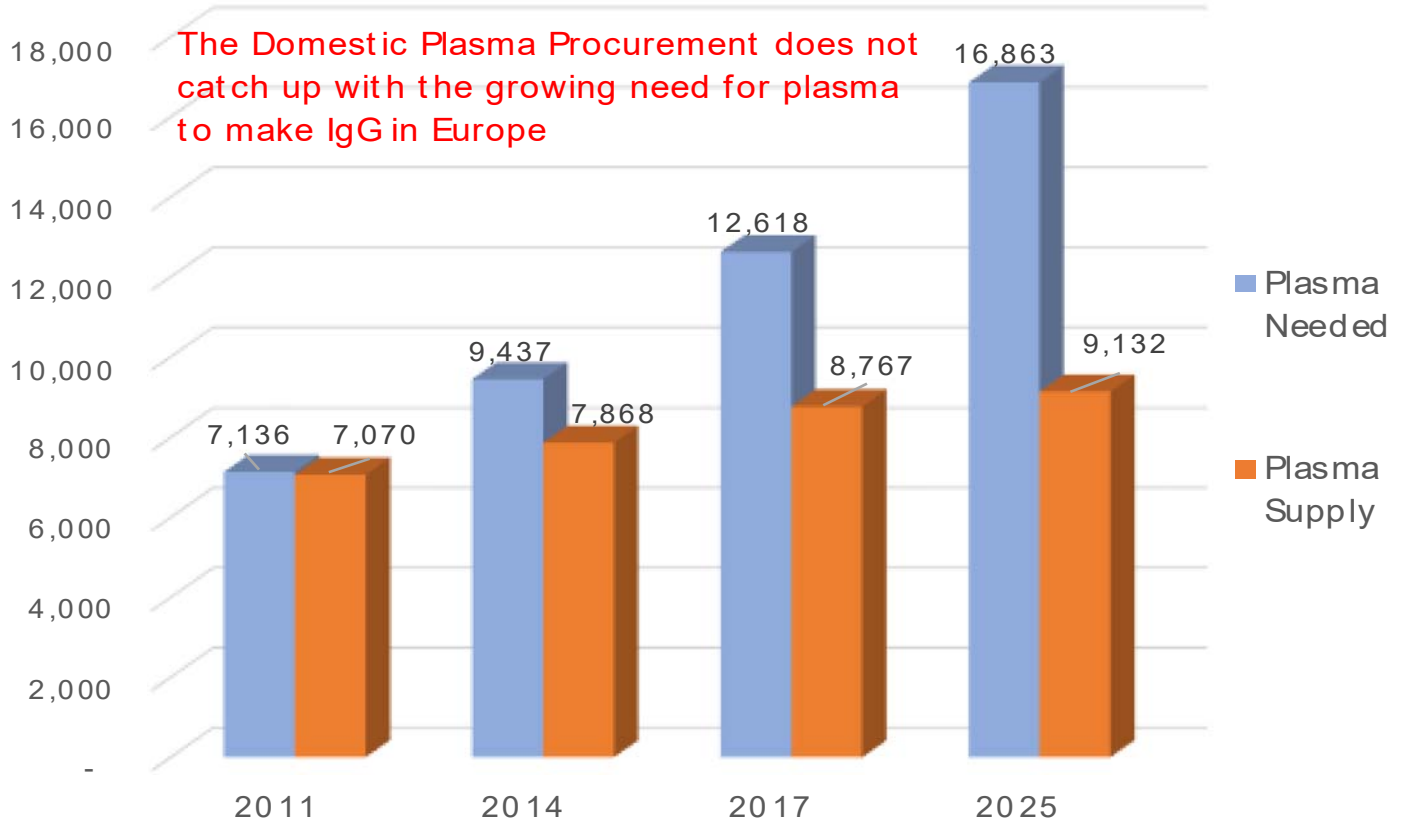
Additional plasma volume required between 2017 and 2025 (liters x 000) 3,880

Assume 9% annual growth of source plasma collections between 2017 and 2025

MRB

Ref. P. Robert, PLUS conference 2019, 24-01-2019

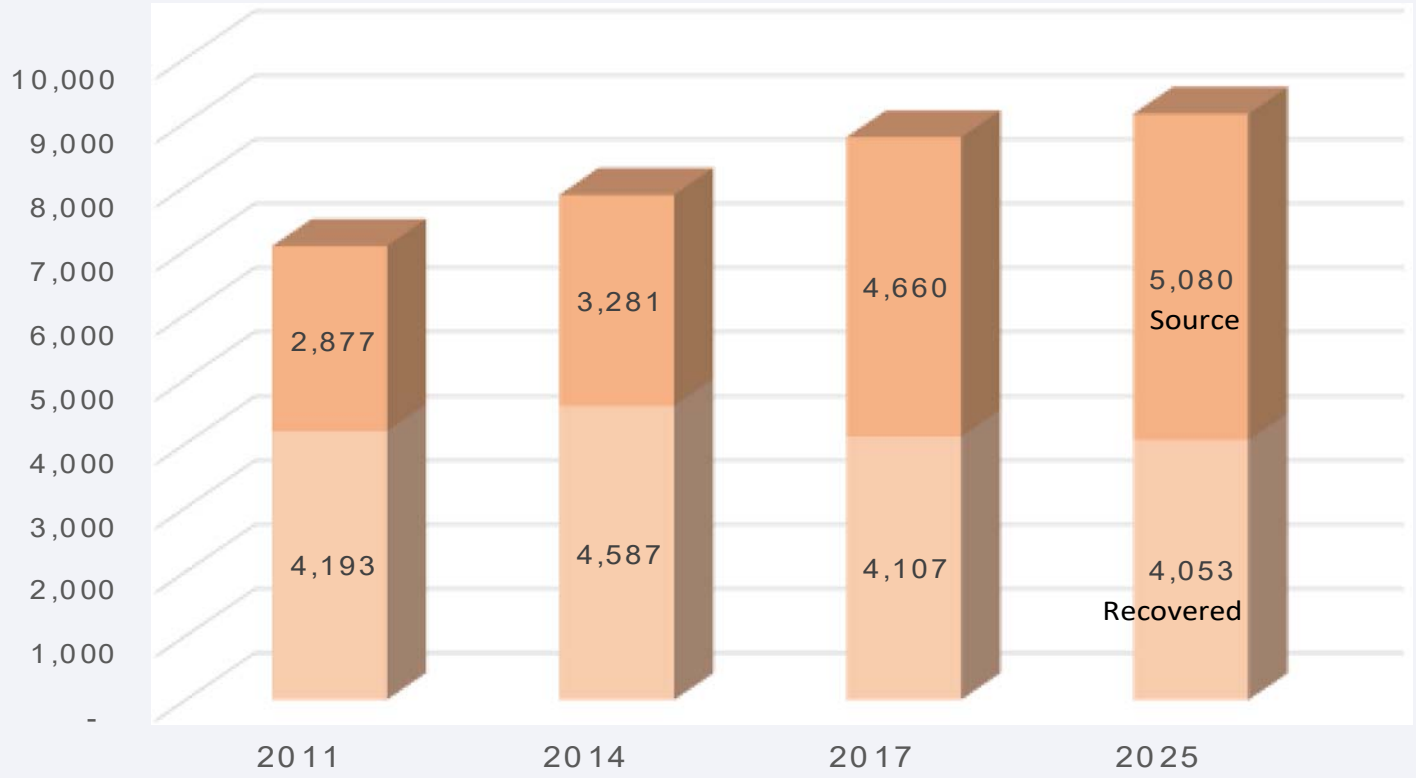
The Growing Discrepancy between the Domestic Supply of Plasma and the Needs to meet IgG Demand from 2011 to 2025



Ref. P. Robert, PLUS conference 2019, 24-01-2019

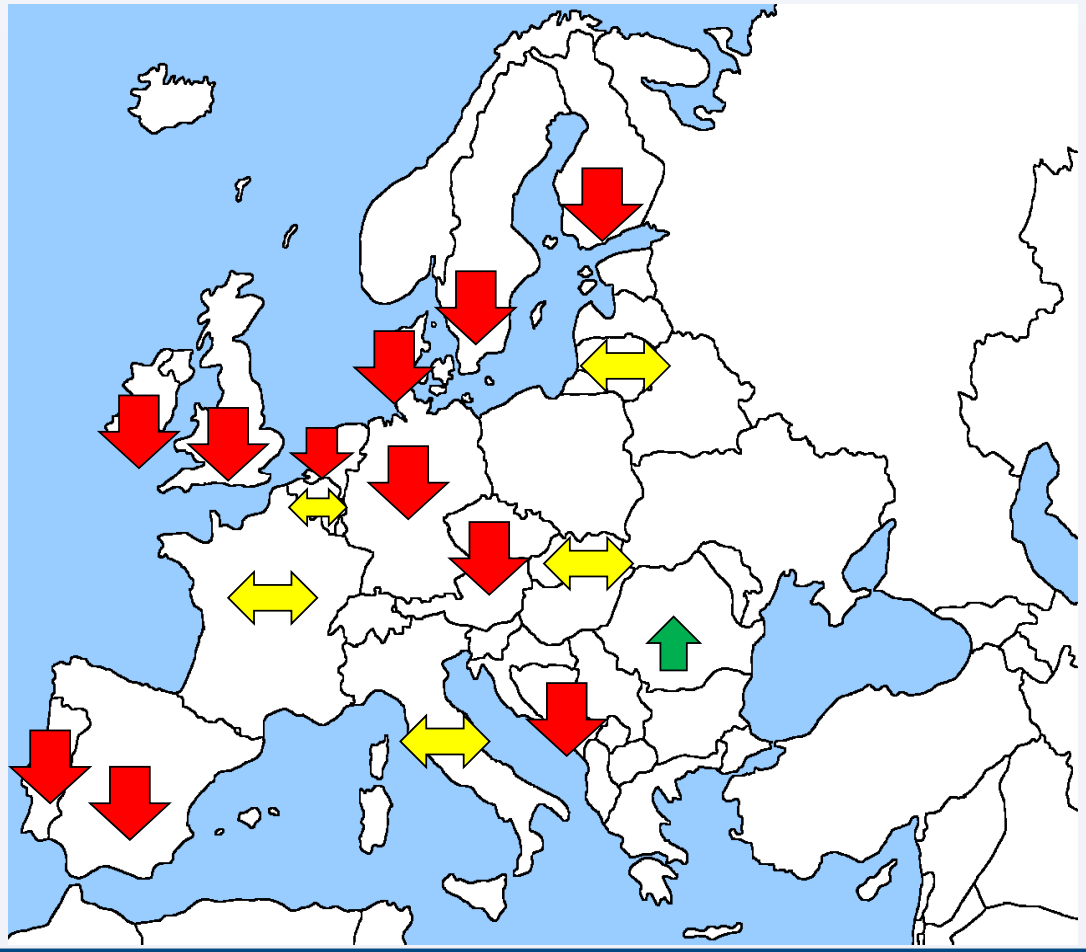
The Growing Discrepancy between Recovered and Source Plasma in the Domestic Supply from 2011 and 2025

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



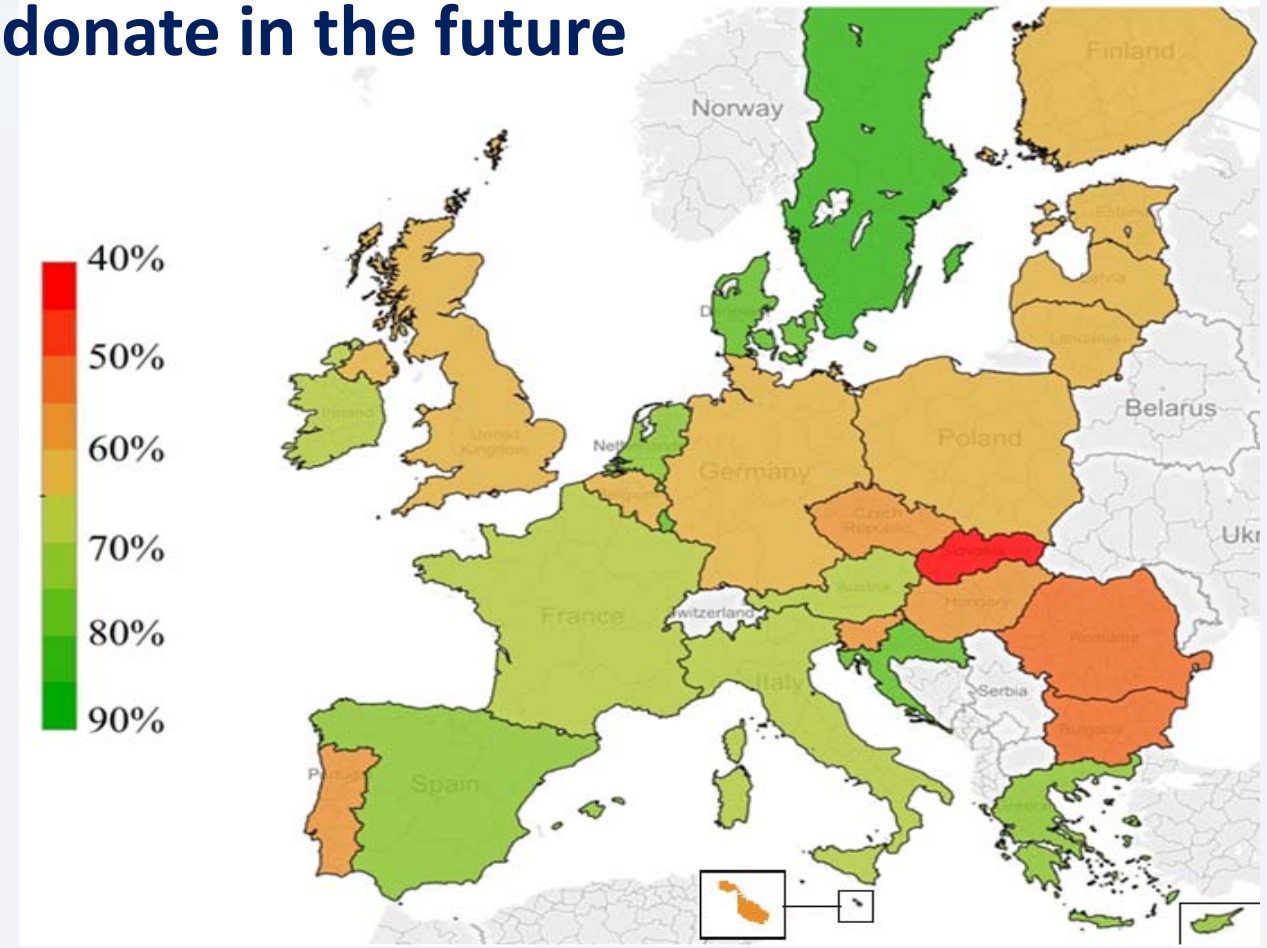
Ref. P. Robert, PLUS conference 2019, 24-01-2019

Number of registered blood donors in European countries



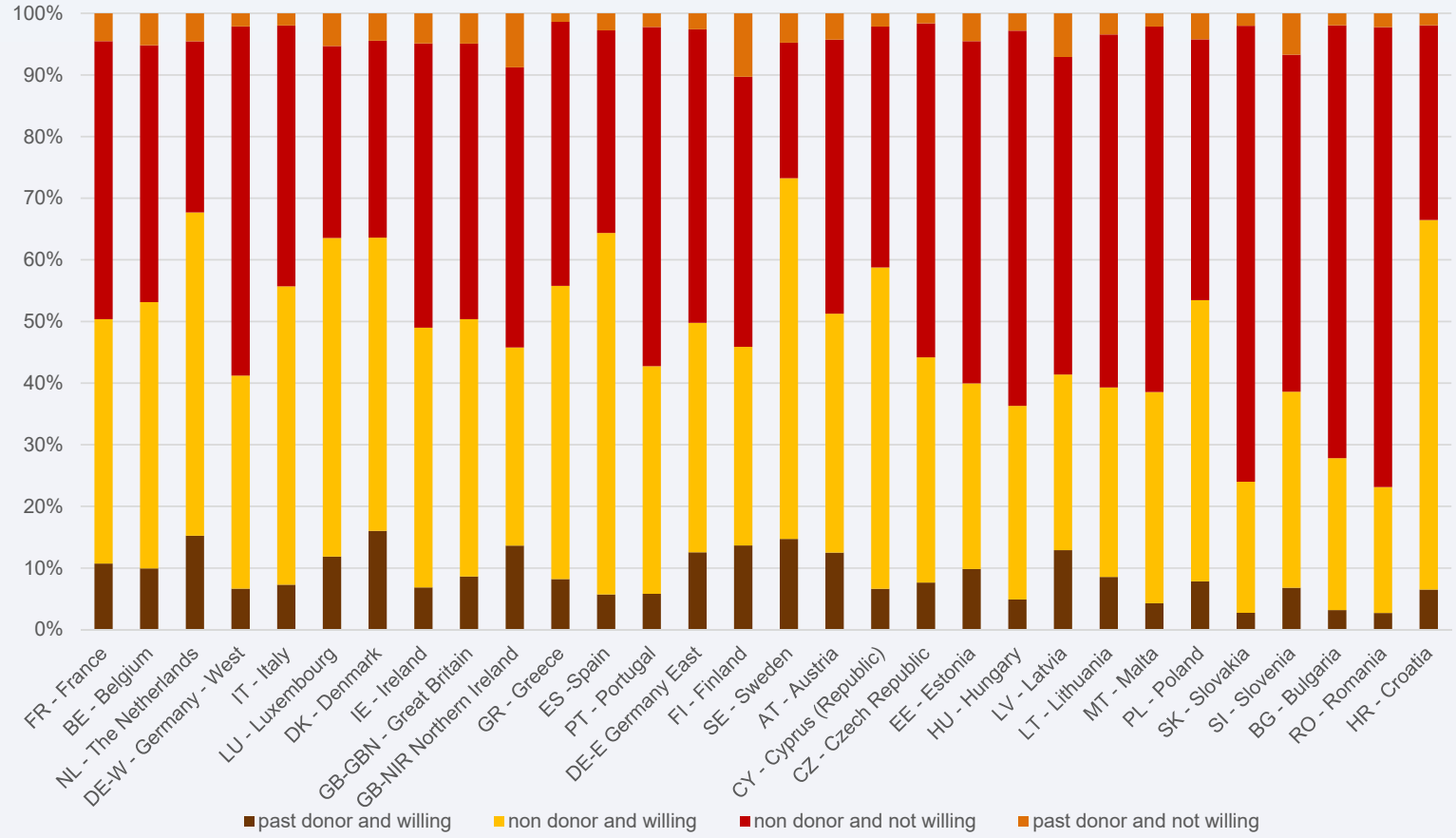
Ref.: European Blood Alliance report, 2015

Willingness to donate in the future



Source: Eurobarometer 2014
(N= 27,868, in 28 countries) Huis in 't Veld, De Kort, Merz 2016

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 prioterise 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"

Alice Simonetti
IFBDO/FIODS
Strasbourg, 29-30/01/19

THE IFBDO

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 valutes 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

THE ACT 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.

THE BLOOD SYSTEM

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.

PROPOSALS

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.

FIODS
NEITHER RACE NOR RELIGION OR BORDERS

edqm

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

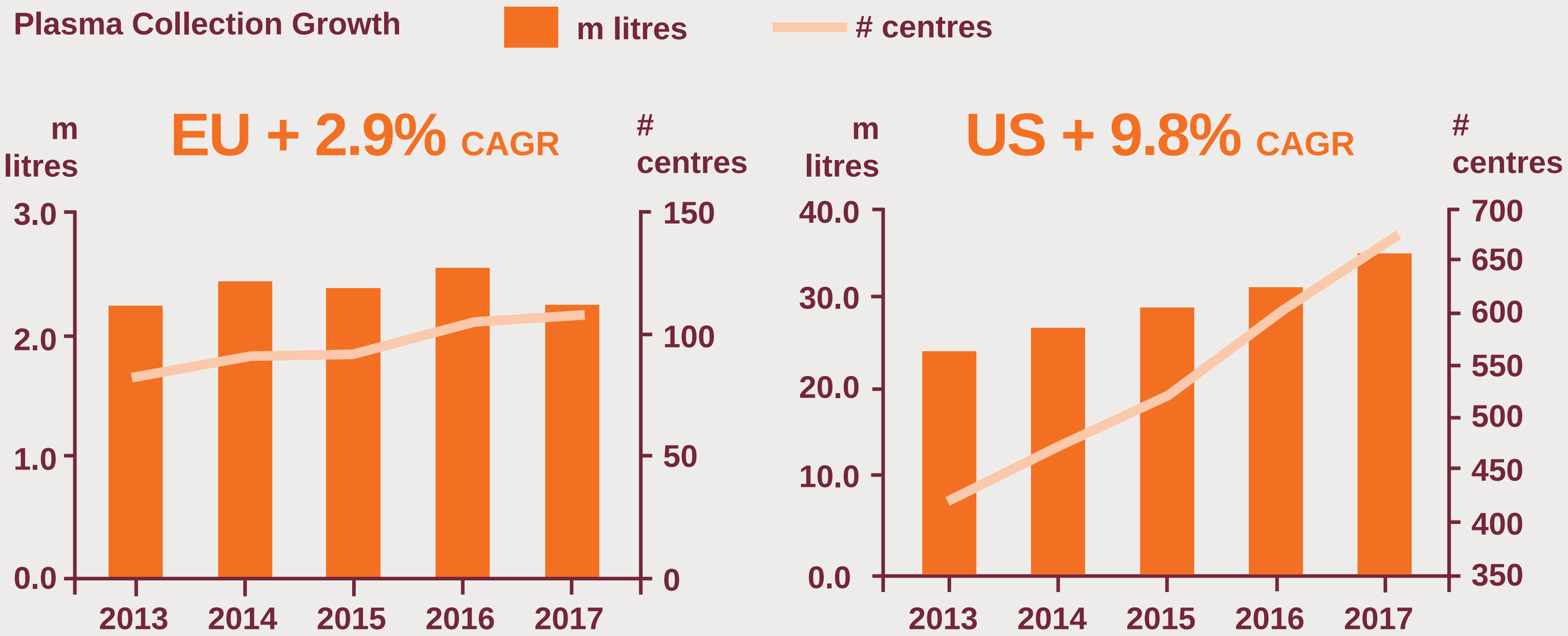
Member Executive Board - Director Blood Bank

Sanquin

Background (1)

Increasing dependency on US plasma

Plasma Collection Growth



Source: Company information, equity research, Grifols analyst presentations

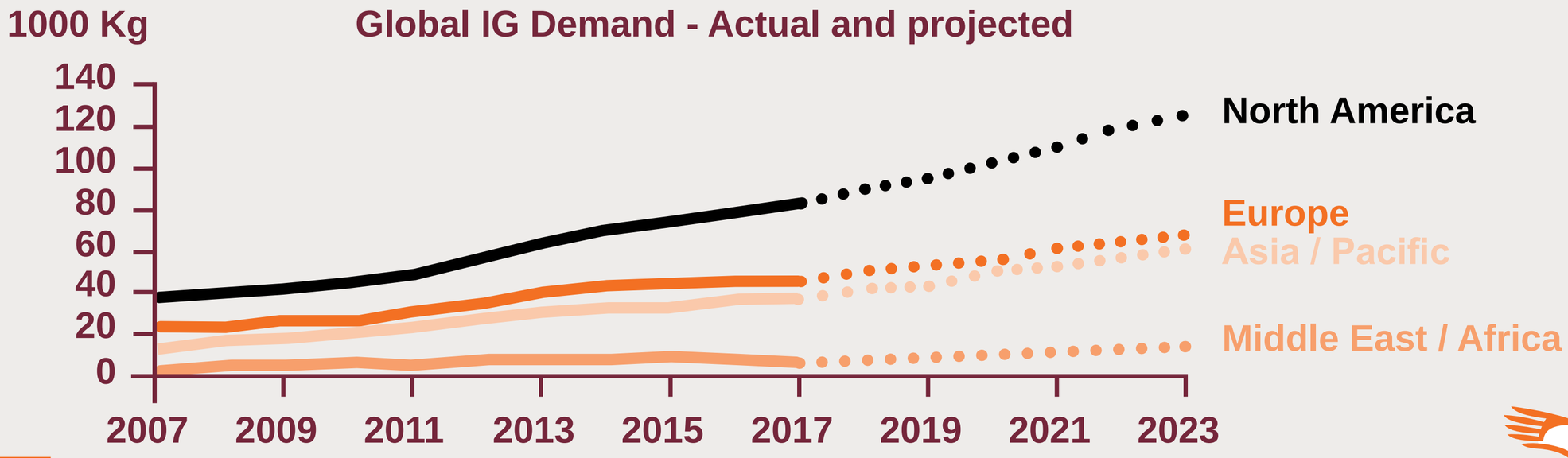
Background (2)

- Decrease in recovered plasma
- Growing demand for source plasma
- Plasmapheresis is not costefficient

Need for more plasma donors who donate more frequently

Guiding principles:

- donor safety
- voluntary non remunerated



Source: Company information, equity research, Grifols analyst presentations

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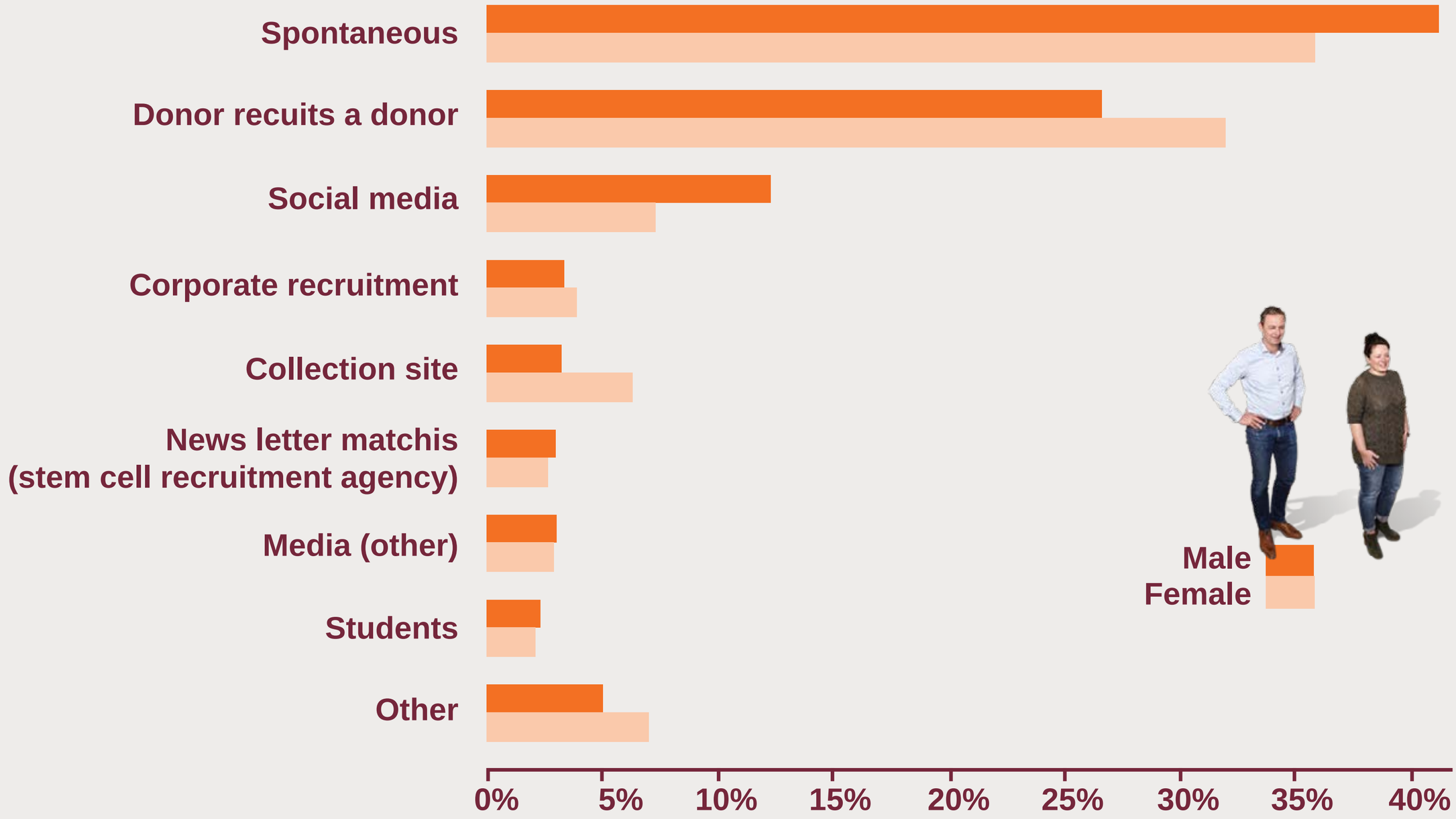
Donor recruitment channels

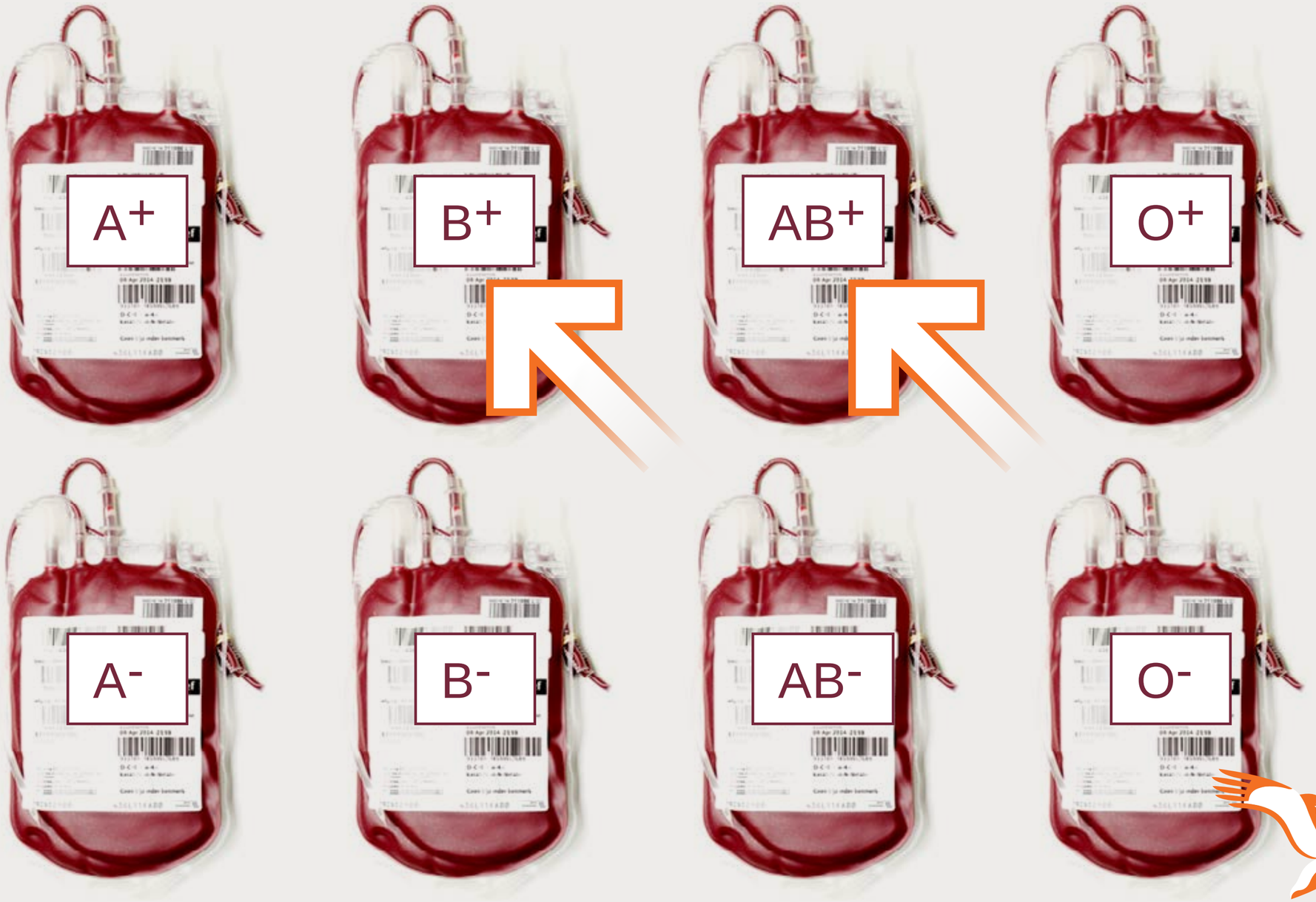
Registration new donors @Sanquin (2018)



Plasma donor recruitment

@ Sanquin

Converting B+ and AB+ whole blood donors in plasmapheresis donors



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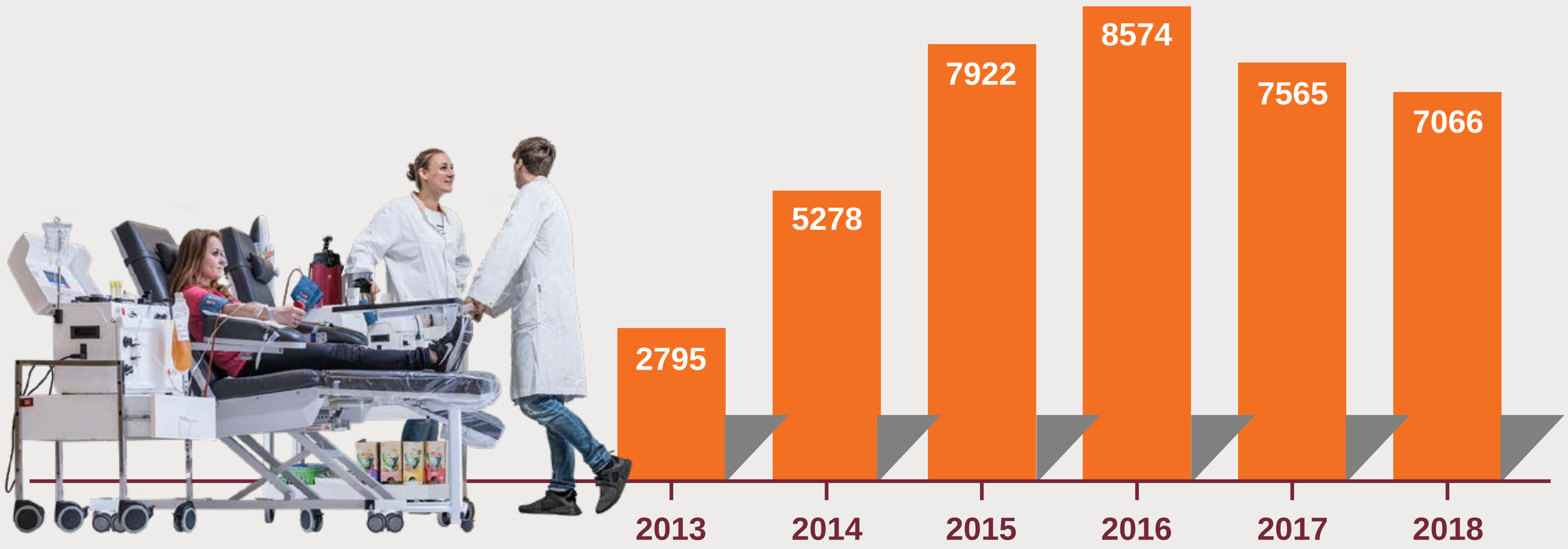
Plasma donor recruitment

@ Sanquin

first time plasma donors



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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

Sanquin

Qualitative research

Motives of donors & non-donors

30 IN-DEPTH INTERVIEWS

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

08:00

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**

14:00

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

Qualitative research

Motives of donors & non-donors

30 IN-DEPTH INTERVIEWS

Key information:

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

18:00

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

Qualitative research

Motives of donors & non-donors

30 IN-DEPTH INTERVIEWS

Key information:

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

20:00

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

Qualitative research

Motives of donors & non-donors

30 IN-DEPTH INTERVIEWS

Key information:

Donating for a good cause

interferes with the ‘commercial interest’

of producing medicines

12

21:00

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

Qualitative research

Motives of donors & non-donors

30 IN-DEPTH INTERVIEWS

“When I think about manufacturing pharmaceuticals, I do think of big money making machines”
(F, 36, ex-donor, Amsterdam)

Key information:

More plasma donors would like

a **form of compensation**

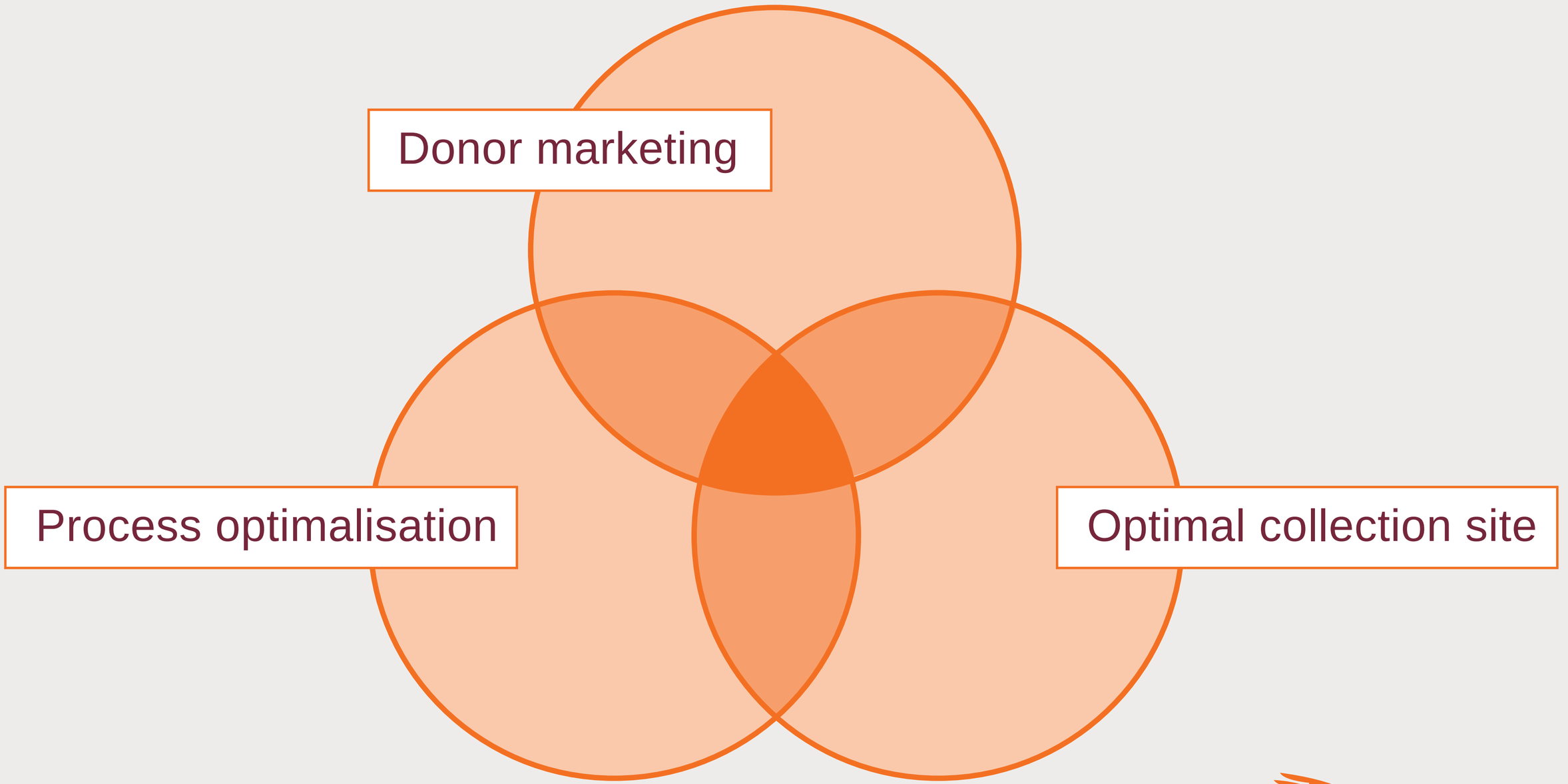
when asked to donate more often

22:00

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

InPlace

a pilot center for cost efficient plasma collection



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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?

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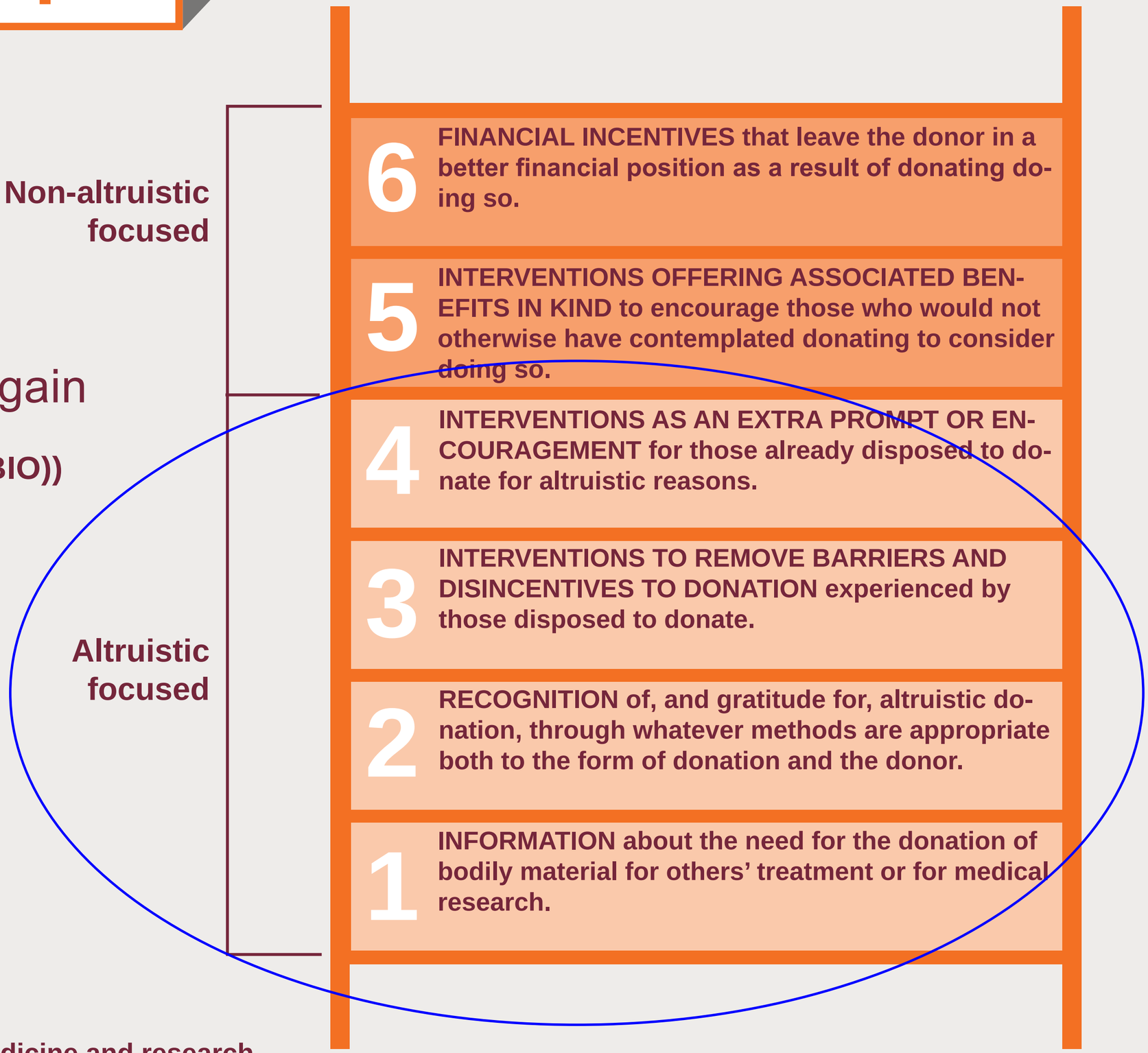
Guiding principle

The principle of the prohibition of financial gain

(Committee on Bioethics (DH-BIO))

An intervention Ladder for promoting donation



Source: Human bodies: donation for medicine and research, Nuffield Council on Bioethics

Plasma donors

in The Netherlands

Method:

- Use of Dutch consumer data (WHOOZ)
- Different segments based on wealth and age
- Defining current plasma donor population
- Defining target population plasma donors

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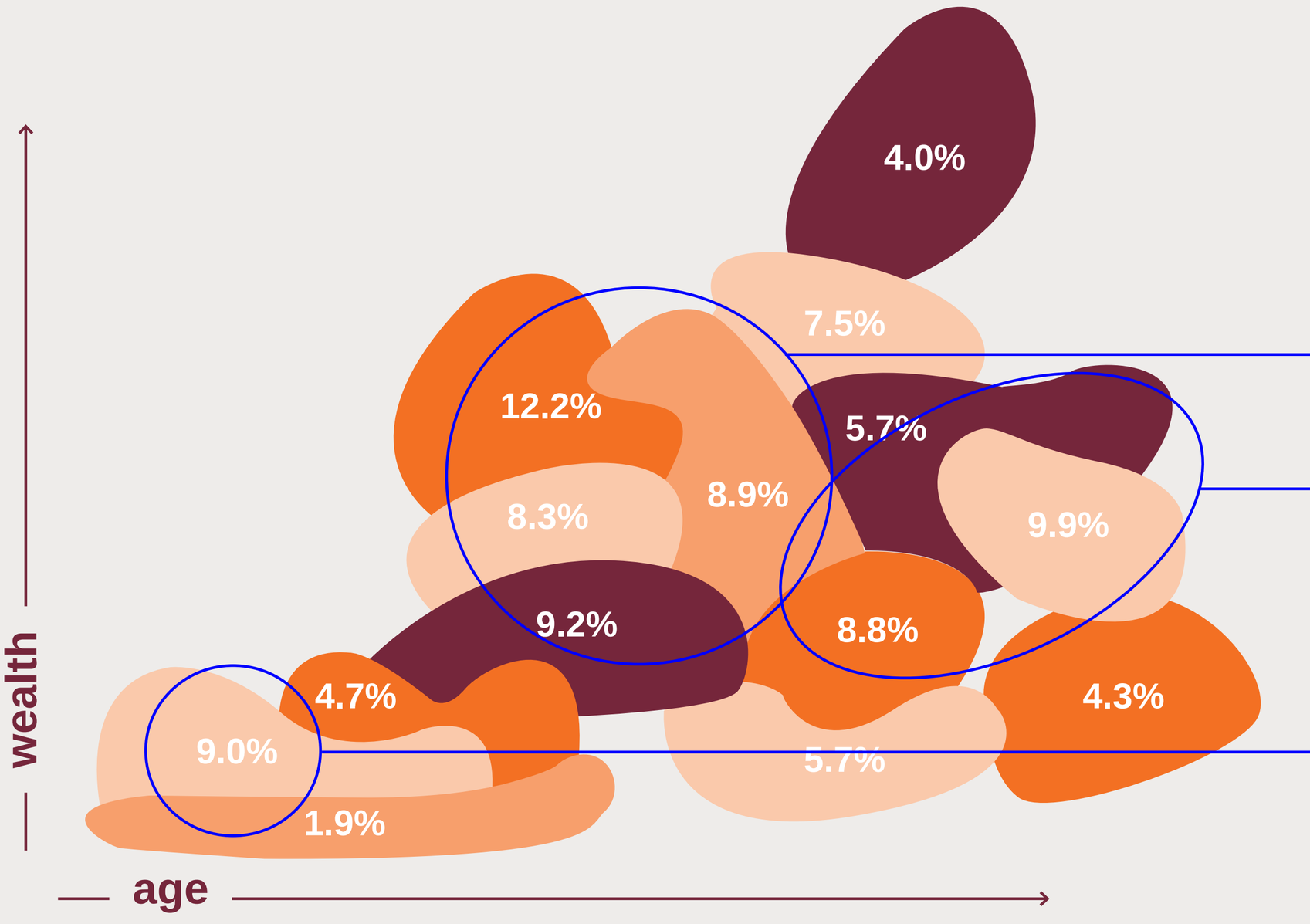
Results

plasma donors in The Netherlands



Highly represented within current population

Age 30-55; mid- high educated

Age 55+; average income

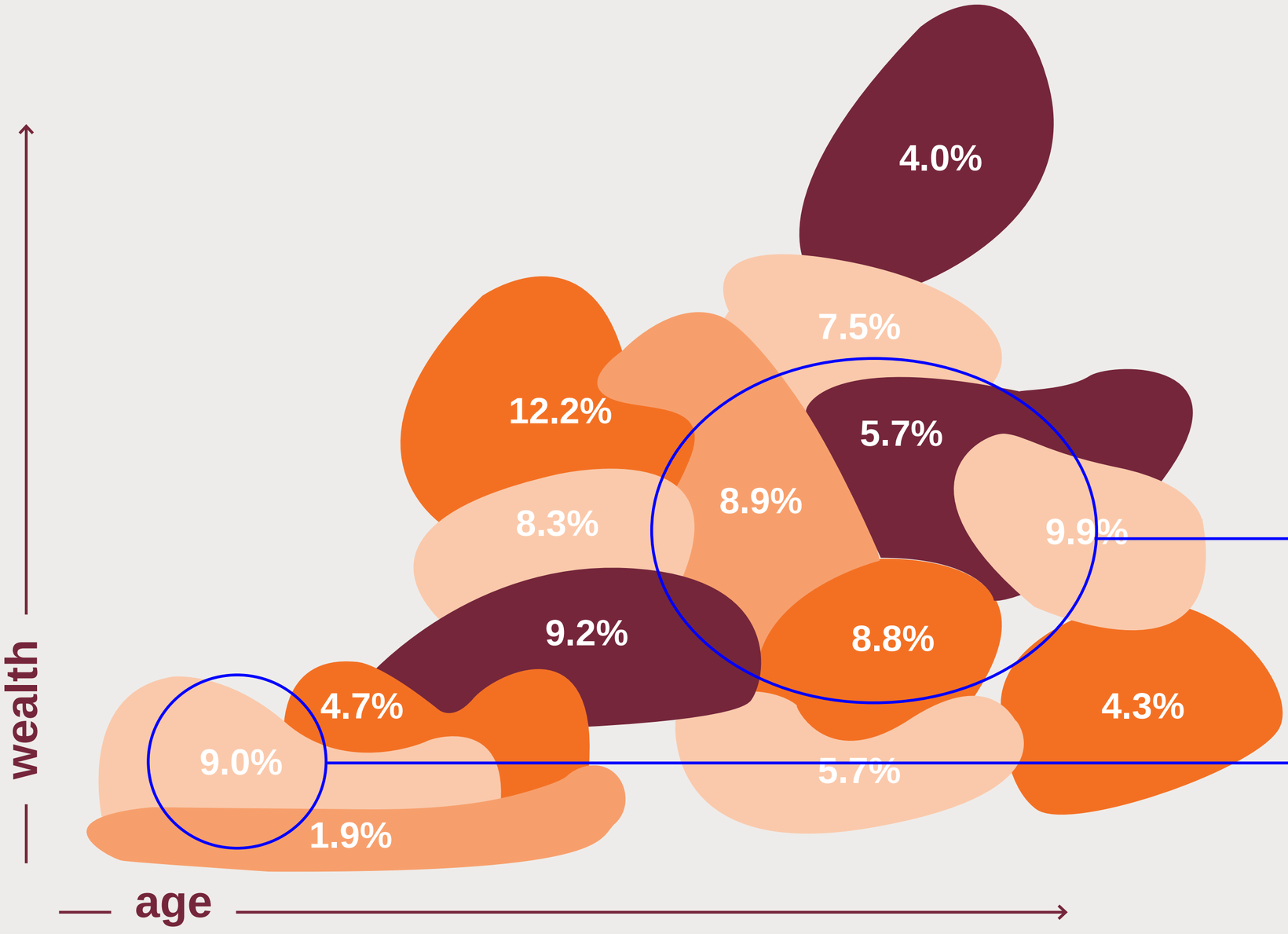
Students

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

Sanquin

Results

plasma donors in The Netherlands



Donation frequency

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

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

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

Sanquin

InPlace

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**

Sanquin

InPlace

Time line

Communication external & internal stakeholders

What	When
Define geographic location	Jan 2018
Impact analysis on whole blood donors (surroundings of defined location)	Feb 2018
Plasma Donors Journey	Feb-Mar 2018-2019
Proposals for recruitment strategy	Mar-Apr 2019
Procurement of machines, test, beds, etc.	Mar-May 2019
Start donor recruitment	May 2019
Official opening of center	Sep 1st 2019
Evaluation of first results	Jan-Mar 2020

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

Sanquin

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

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

Sanquin

ETABLISSEMENT FRANÇAIS DU SANG

Symposium on Plasma Supply Management
29-30 January 2019
EDQM - Strasbourg

LEARNINGS FROM THE FRENCH ATTEMPT TO CONVERT WHOLE BLOOD DONORS IN PLASMAPHERESIS DONORS

Dr Frédéric Bigey

BACKGROUND

French context :

- **Etablissement Français du Sang (EFS) :** monopolistic national public blood service, organized in 10 metropolitan regions + 3 overseas.

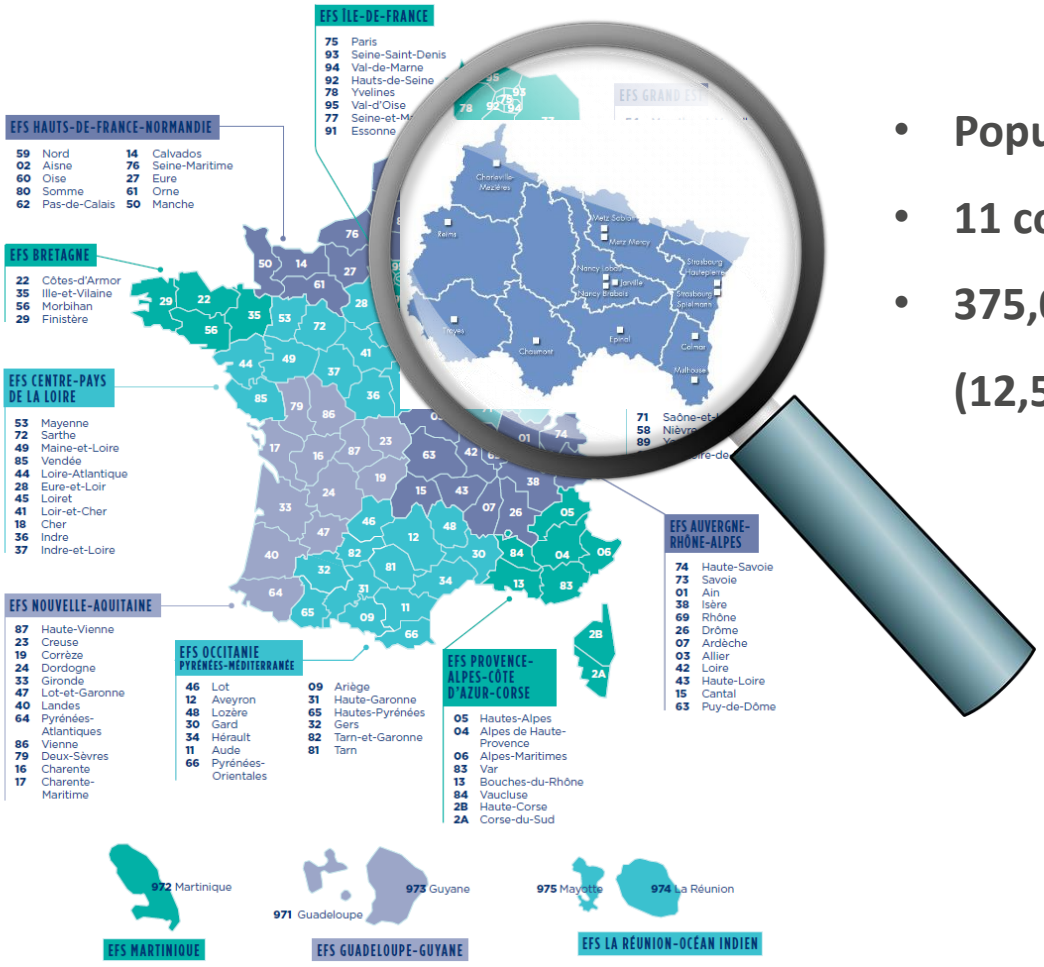
- **Laboratoire du Fractionnement et des Biotechnologies (LFB)** : private plasma fractionator with 100% public funds, has the obligation to fractionate the plasma collected by EFS.

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

LFB plasma demand	Global plasma volume (L)			additionnal plasmapheresis	% increase
	TOTAL	Recovered	Apheresis		
2016	854,500	600,443	254,057	-	-
2017	894,500	605,209	289,291	50,877	14%
2018	934,500	592,747	341,753	75,067	18%
2019	974,500	581,579	392,921	73,250	15%
2020	991,500	570,623	420,877	40,657	7%

EXPERIENCE OF GRAND EST

EFS



3 million donations/year

EFS Grand Est (GEST)

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

  (12,5% of national)

GENERAL ORGANIZATION

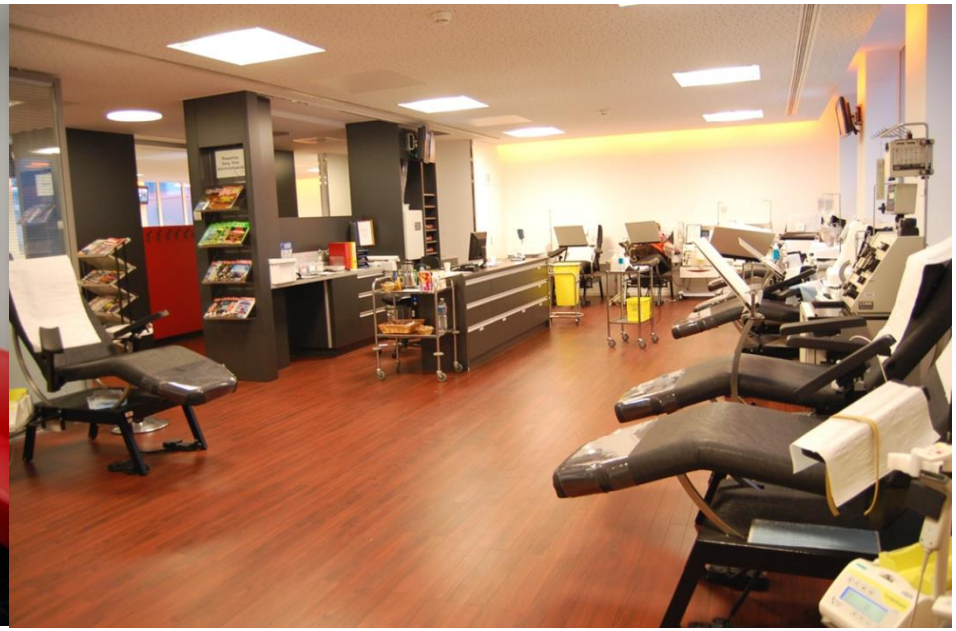
- 11 plasmapheresis sites

- 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

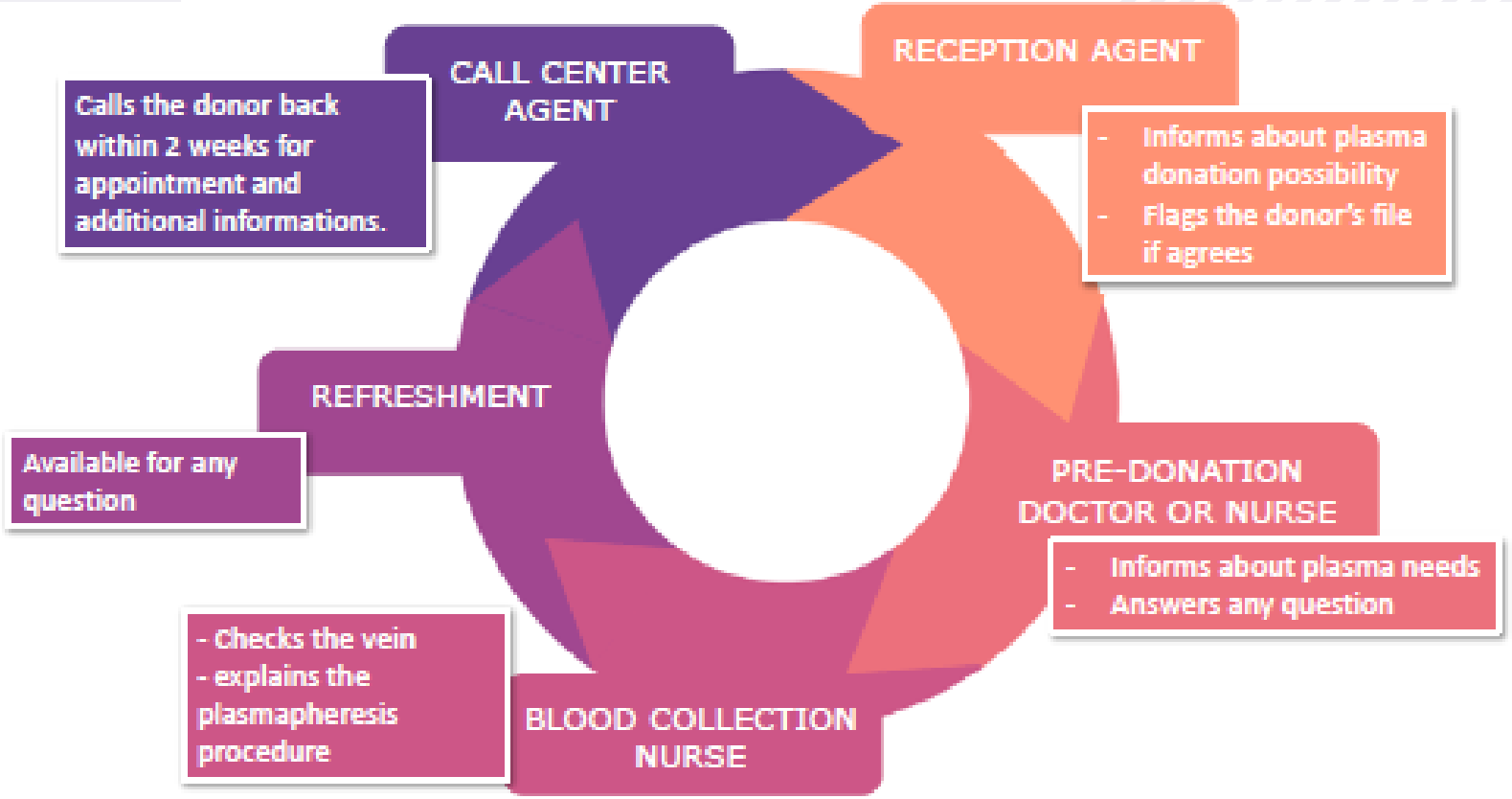
- **Call center** capacity

  → Annual plan to increase plasmapheresis for each site

  Objective : 74,480 plasmapheresis in 2017

PLASMA CONVERSION : A TEAM CHALLENGE

- Conversion from **mobile session** : a virtuous circle



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

- Conversion **on-site** from WB donors

PLASMA RECRUITMENT LEAFLET 1/2

PASSEZ À L'ACTION
ET DONNEZ VOTRE PLASMA !

Prenez rendez-vous dès maintenant auprès de nos équipes ou sur le site mon-rdv-dondesang.efs.sante.fr* pour votre prochain don de plasma.

Vous souhaitez être recontacté par l'EFS plus tard ? Remplissez ce formulaire et remettez-le aux équipes sur place.

Mes coordonnées :

Homme Femme

Prénom :

Nom d'usage (marital) :

Nom de naissance :

Adresse :

Code postal : LLLLL

Ville d'habitation :

Téléphone : LL LL LL LL LL

Date de naissance : LL LL LLLL

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 : .....H.....

Commentaire(s) : .....

.....

.....

.....

*service disponible selon les régions indiquées sur le site.

** sous réserve de raccord de la personne en charge de rentrer un prélèvement au don.

OÙ DONNER VOTRE PLASMA ?

Auvergne - Rhône-Alpes : 04 78 65 63 63

Bourgogne Franche-Comté : 0 800 109 000

Bretagne : 02 99 54 42 22

Centre - Pays de la Loire : 0 800 109 000

Grand Est : 0 800 109 000

Hauts-de-France - Normandie : 0 800 109 000

Île-de-France : 0 800 109 000

Nouvelle Aquitaine : 0 800 744 100

Occitanie : 0 800 872 100

Provence-Alpes Côte d'Azur - Corse : 0 800 109 000

Facilitez-vous la vie, prenez rendez-vous ici : mon-rdv-dondesang.efs.sante.fr*

EFS

20, avenue du Stade de France
93210 La Plaine Saint-Denis Cedex
Tél. 01 55 93 55 00
Fax 01 55 93 55 03

dondesang.efs.sante.fr

EFS
Du devoir aux patients

Vivez une nouvelle expérience !
Don de plasma

Sabrina, immunodéprimée

" Petite, j'étais souvent malade jusqu'à ce que mon médecin découvre que j'avais un déficit immunitaire primitif (DIP). Depuis, tous les mois, j'ai des perfusions d'immunoglobulines : c'est un médicament fabriqué grâce à la générosité des personnes qui donnent leur plasma. Grâce à ce traitement - à vie -, je mène une vie normale et même, ... je suis maman ! "

Merci à l'association IRIS pour ce témoignage.

Le don de plasma s'effectue uniquement sur rendez-vous dans un site de prélèvement.

Durée : 1h pour le prélèvement et 1h30 de votre arrivée à votre départ.

Fréquence : 24 fois par an maximum en respectant un délai de 2 semaines entre un don de plasma et tout autre don.

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.

Comment donner son plasma ?

Vous pouvez choisir de donner exclusivement votre plasma en effectuant une « plasmaphérèse ». 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 plasmaphérèse permet de prélever plus de plasma que lors d'un don de sang.

Cette technique est indispensable pour répondre aux besoins des patients, en constante augmentation, notamment pour les maladies auto-immunes dont les maladies rares et orphelines.

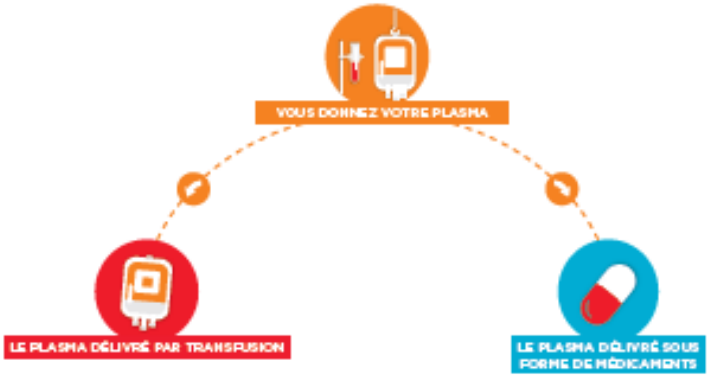
Qui peut donner son plasma ?

Toute personne âgée de 18 à 65 ans reconnue apte à l'issue de l'entretien 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 donneurs universels pour le plasma. En effet, leur plasma peut être transfusé à tous les patients. Seuls 4 % des Français sont de 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.



Qui soigne-t-on ?

Ce plasma est utilisé pour les patients atteints d'hémorragie, mais aussi pour ceux qui subissent une opération de neurochirurgie, de chirurgie cardiaque ou obstétrique.

Comment ça marche ?

Pour être transfusé, le plasma doit passer par une étape de sécurisation. Celle-ci consiste à conserver la poche de plasma dans l'attente d'un autre don qui doit avoir lieu 61 jours au moins après le don initial.

De J+61 à J+120 : c'est la bonne période durant laquelle vous pouvez venir sécuriser votre don initial par un 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 soigne-t-on ?

Ces médicaments sont généralement utilisés pour les patients atteints de maladies chroniques. Certains d'entre eux ont des besoins toutes les 5 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 principales sont :

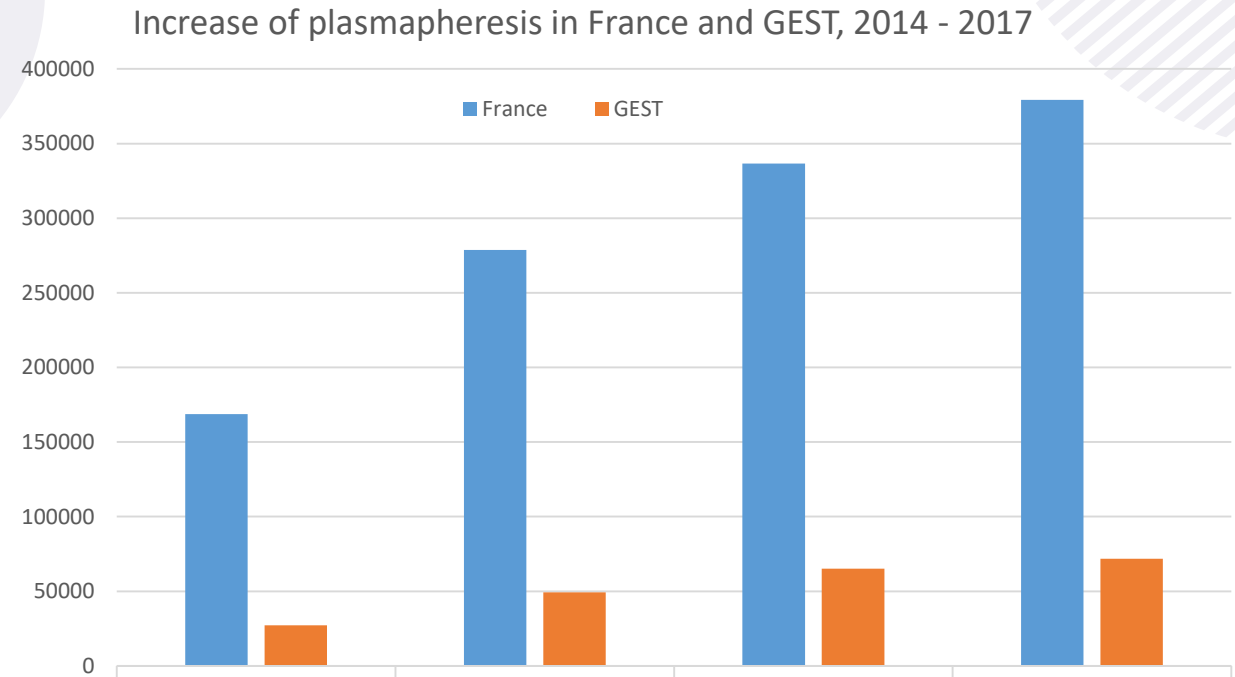
- **L'albumine →** pour la prise en charge des grands brûlés, des blessés graves et des patients en réanimation.
- **Les immunoglobulines →** pour les patients atteints de déficits immunitaires et de certaines maladies auto-immunes.
- **Les facteurs de coagulation →** pour les maladies hémorragiques comme l'hémophilie.

Vacciné contre l'hépatite B ou le tétanos ? Parlez-en lors de l'entretien préalable au don.

Vous avez développé des anticorps protecteurs contre ces maladies. Votre don de plasma est donc indispensable à la fabrication de médicaments. Ces derniers sont utilisés pour le traitement préventif des personnes exposées à l'hépatite B (les nouveaux nés dont la mère est porteuse du virus, les patients hémodialysés, ceux greffés du foie…) ou au tétanos.

RESULTS

Plasma donations in France and GEST, 2014 → 2017



	2014	2015	2016	2017
France	168730	278750	336509	379 284
GEST	27120	49177	65192	71856

France : + 125%,

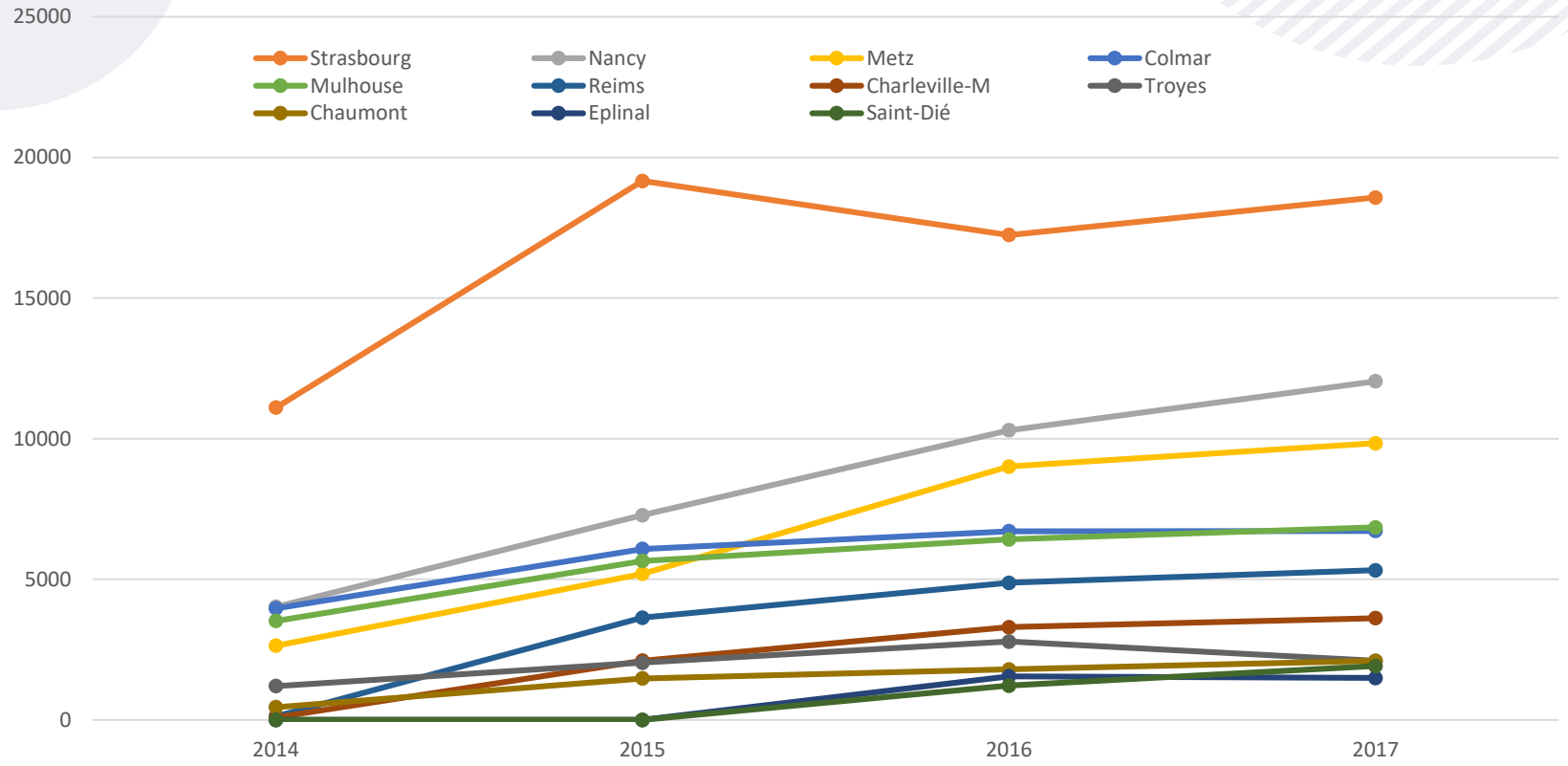
GEST : +165%, 19% of plasmapheresis in France

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

KEY INDICATORS

2017	Nb of plasma donors	GI	% new donors	LI	% plasma donors /all donors
GEST	22138	0.63%	25%	3.64	12.6%
Strasbourg	5950	0.88%	28%	3.36	15.4%

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

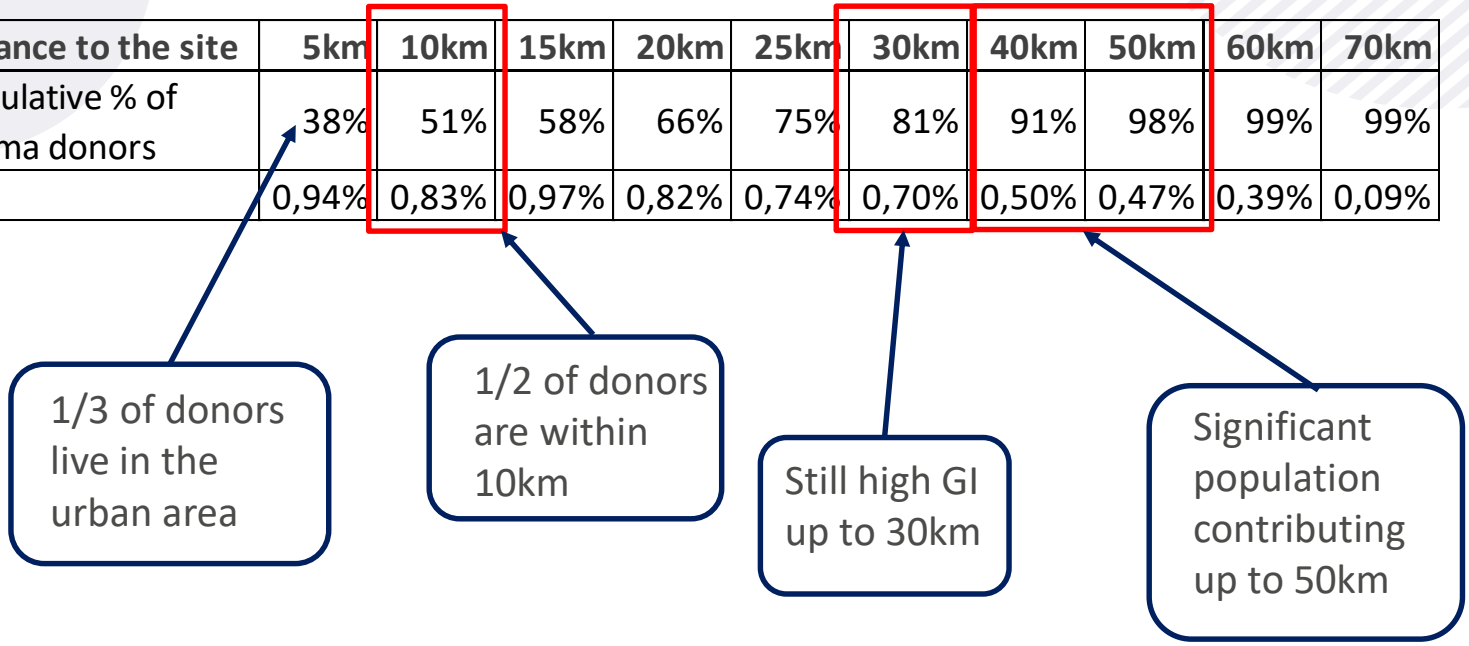
Best indicators for Strasbourg (except the LI)

GI overall : 4.6 %

GEOGRAPHY

Plasma donors and distance to the site, Strasbourg example

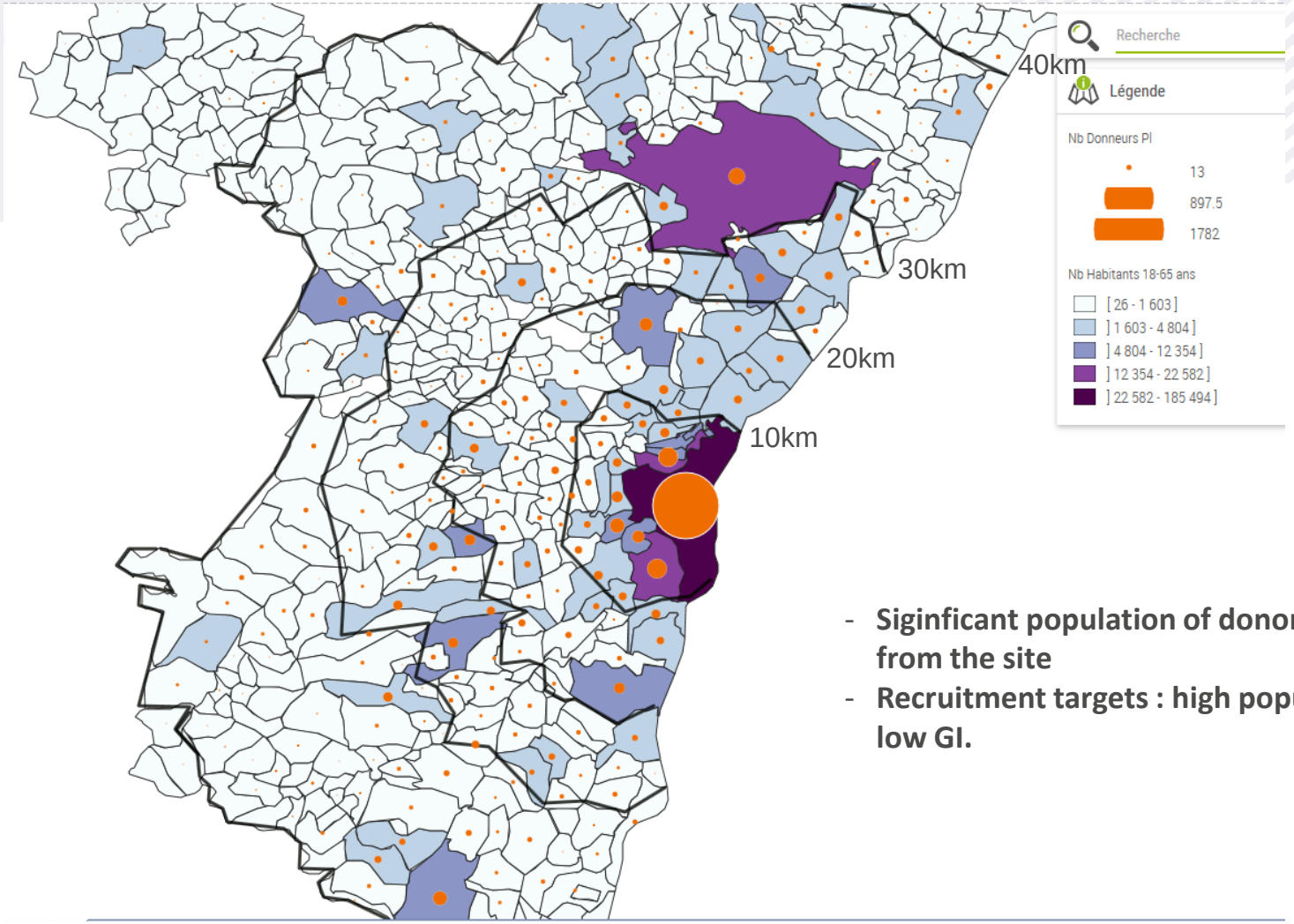
Distance to the site	5km	10km	15km	20km	25km	30km	40km	50km	60km	70km
Cumulative % of plasma donors	38%	51%	58%	66%	75%	81%	91%	98%	99%	99%
GI	0,94%	0,83%	0,97%	0,82%	0,74%	0,70%	0,50%	0,47%	0,39%	0,09%



Recruitment/conversion : no stringent distance limit to be applied

GEOGRAPHY

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



- **Siginficant population of donors away from the site**
- **Recruitment targets : high population, low GI.**

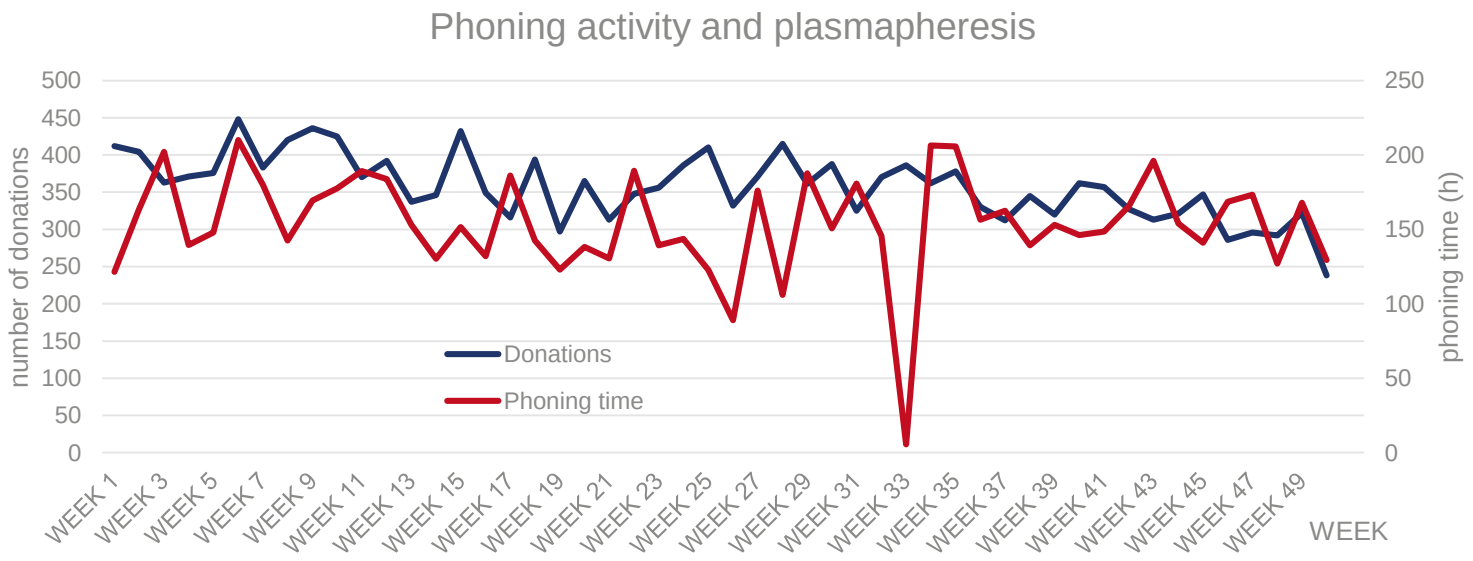
CALL CENTER SUPPORT

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 reliancy for appointments



30% of donors book on-site for their next donation

PROSPECTIVE

If Strasbourg performance rates applied to other sites of GEST :

- **GI (recruitment, conversion) → 30,000 donors**
- **% plasma donors (conversion) → 26,000 donors**
- **With regional LI 3.6 : → 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 → 1,000,000 plasmapheresis/year**
- **% plasma donors 11.5 to 15.4% → 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 developped
- 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**?

CONCLUSION

- **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.**

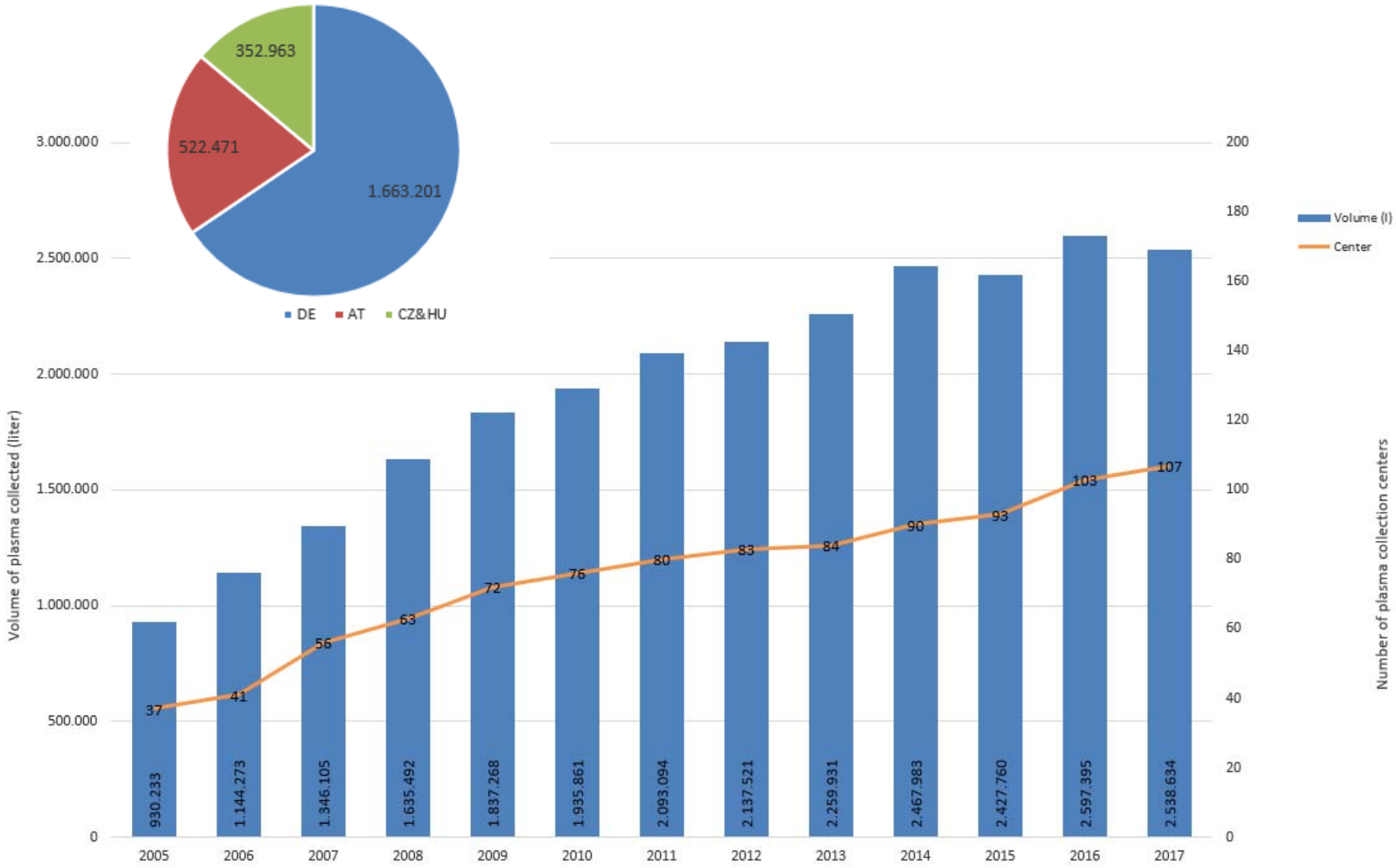
Thank you for your attention !

PPTA
Plasma Protein Therapeutics Association

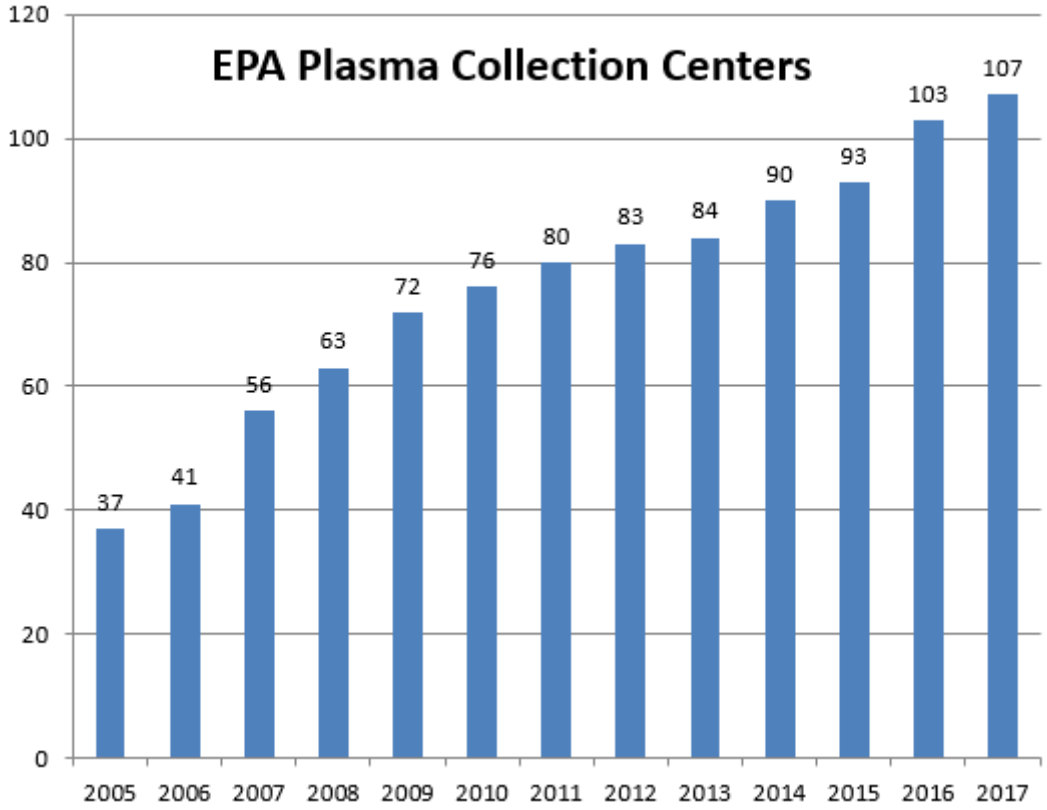
Donor Motivation: EU Plasma Center Experiences

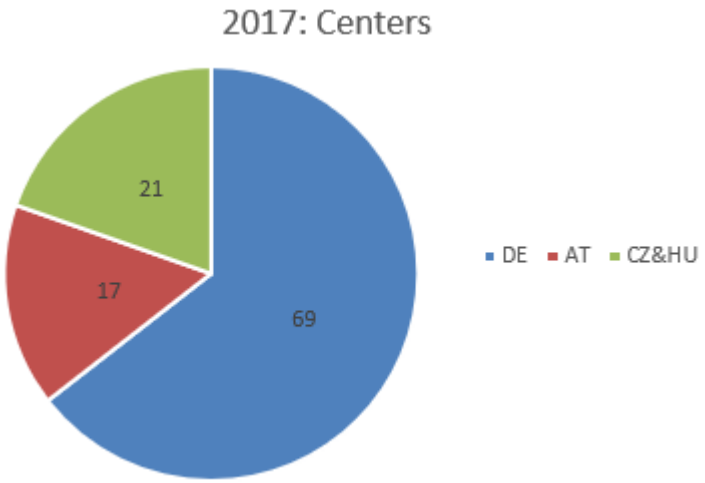
EDQM
January 2019

Yearly Overview 2005-2017



Number of EPA plasma centers 2005 – 2017





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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.**

The Myth of the "Average" Donor

- 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.

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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.

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Generations

- 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**

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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.

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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

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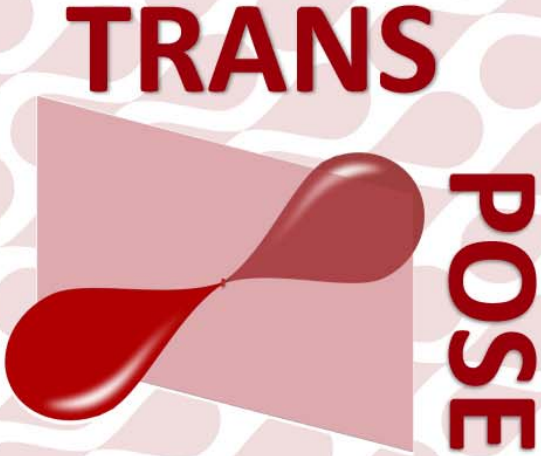
Focus on the Patient

- 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

Co-funded by
the Health Programme
of the European Union

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

WP Number	WP Title	Lead Beneficiary
WP1	Coordination of TRANSPOSE	Sanquin Blood Supply
WP2	Dissemination of the results of TRANSPOSE	Centro Nazionale Sangue
WP3	Evaluation of TRANSPOSE	Établissement Français du Sang
WP4	Inventory of Donor Selection & Protection Practices	University of Cambridge
WP5	Development of Donor Selection & Protection Guidelines	Region Hovedstaden Denmark
WP6	Development of a Standard Donor Health Questionnaire	University of Hamburg
WP7	Training Course/Workshop on the Use of the Guiding Principles	Établissement Français du Sang

 This presentation is part of the project '738145/TRANSPOSE' which has received funding from the European Union's Health Programme (2014-2020)

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 Hovedstaten 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
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 This presentation is part of the project '738145/TRANSPOSE' which has received funding from the European Union's Health Programme (2014-2020)

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

RECOVERED PLASMA FOR FRACTIONATION

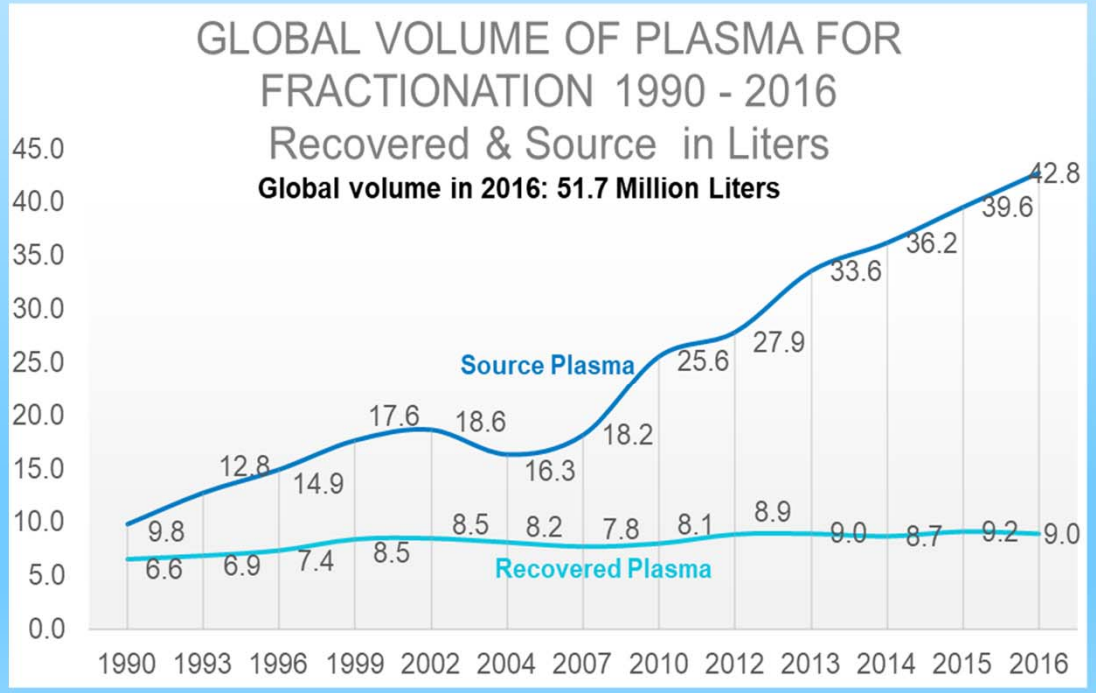
The goal of today speech is to discuss:

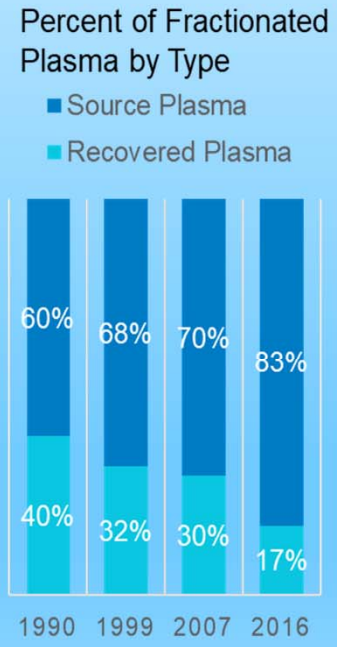
1. How could recovered plasma be used to its full potential for fractionation
2. Proposals for a way forward to intensify recovered plasma collection
3. The obstacles to strategic independence of plasma for fractionation in Europe
4. Whether the EU legislation itself could be perceived as a barrier to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

RECOVERED PLASMA FOR FRACTIONATION

1) How could recovered plasma be used to its full potential for fractionation

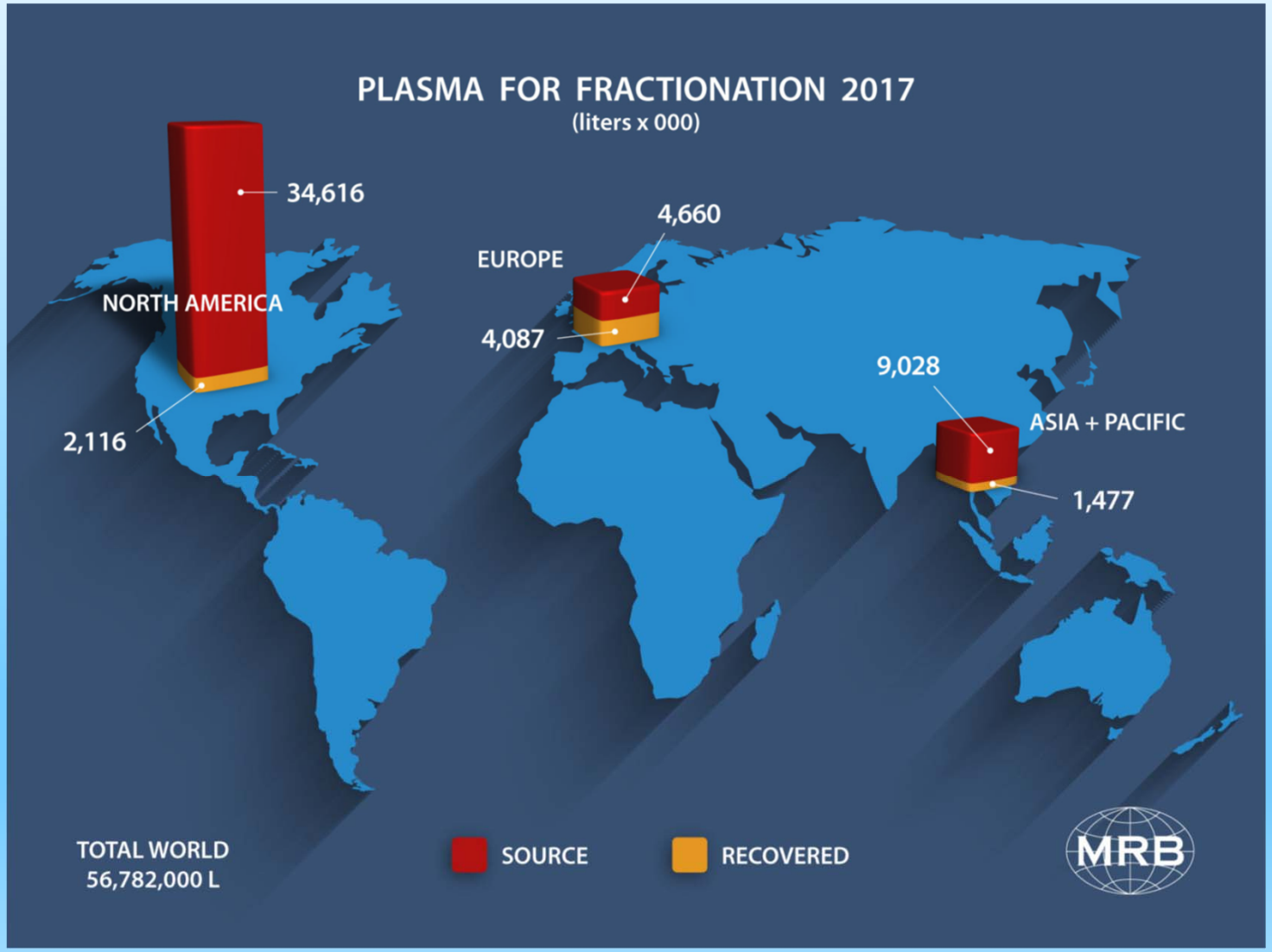
The reality is that in 2018, Recovered Plasma (RP) represents only 15% of the Plasma for Fractionation (PfF) used worldwide





1990-2016 WW Plasma Annual Growth: Source 5.8% Recovered 1.2%

PLASMA COLLECTIONS



Europe has the highest portion of RP been fractionated

Limited room for improvement!

RECOVERED PLASMA FOR FRACTIONATION

What about the rest of the world?

Estimated blood donations by WHO region, 2013

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

Global status report on blood safety and availability 2016!!

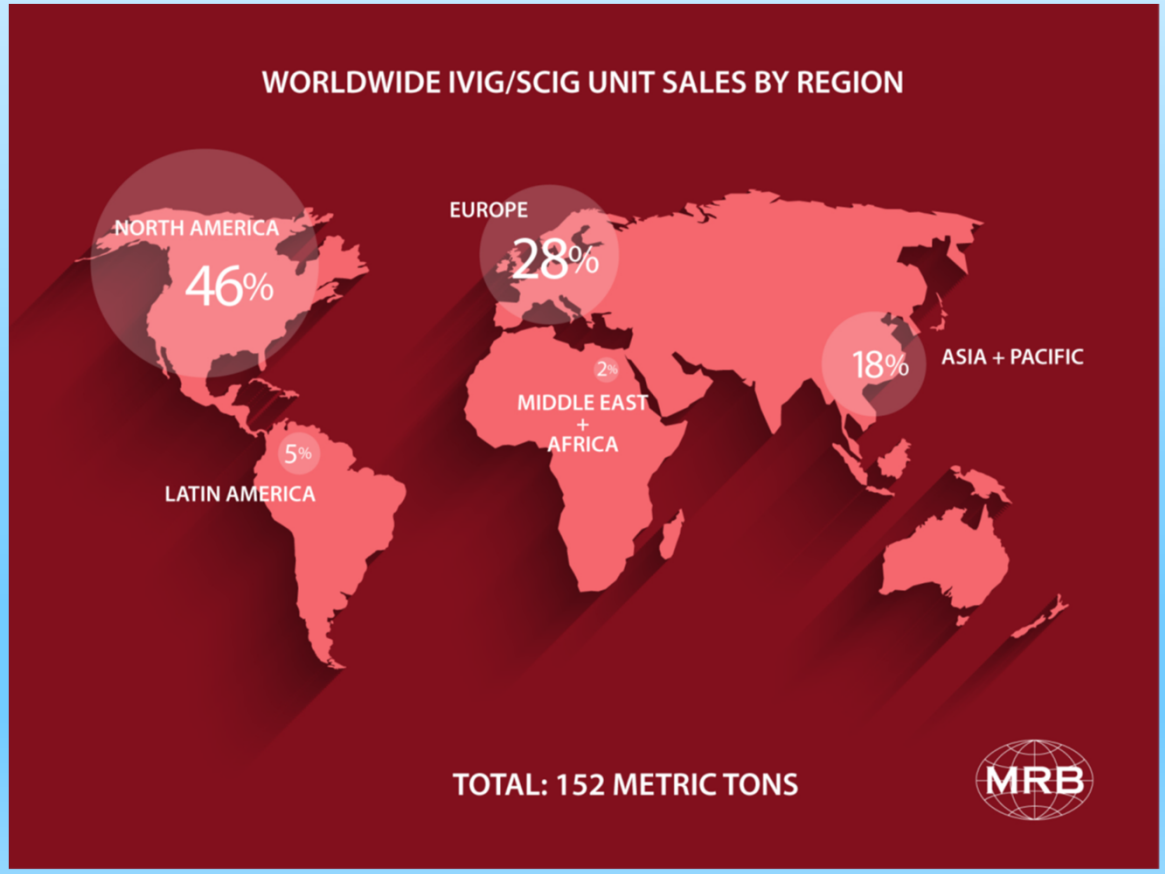
Partly incorrect data. Further, data shows huge discrepancies amongst regions.
Donations in Asia ≠ Europe (average 300 ml versus 500 ml)
9 mio l unused RP as claimed by WHO (really true? Why?)

RECOVERED PLASMA FOR FRACTIONATION

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!



RECOVERED PLASMA FOR FRACTIONATION

1) *How could recovered plasma be used to its full potential for fractionation*
2) Proposals for a way forward to intensify recovered plasma collection

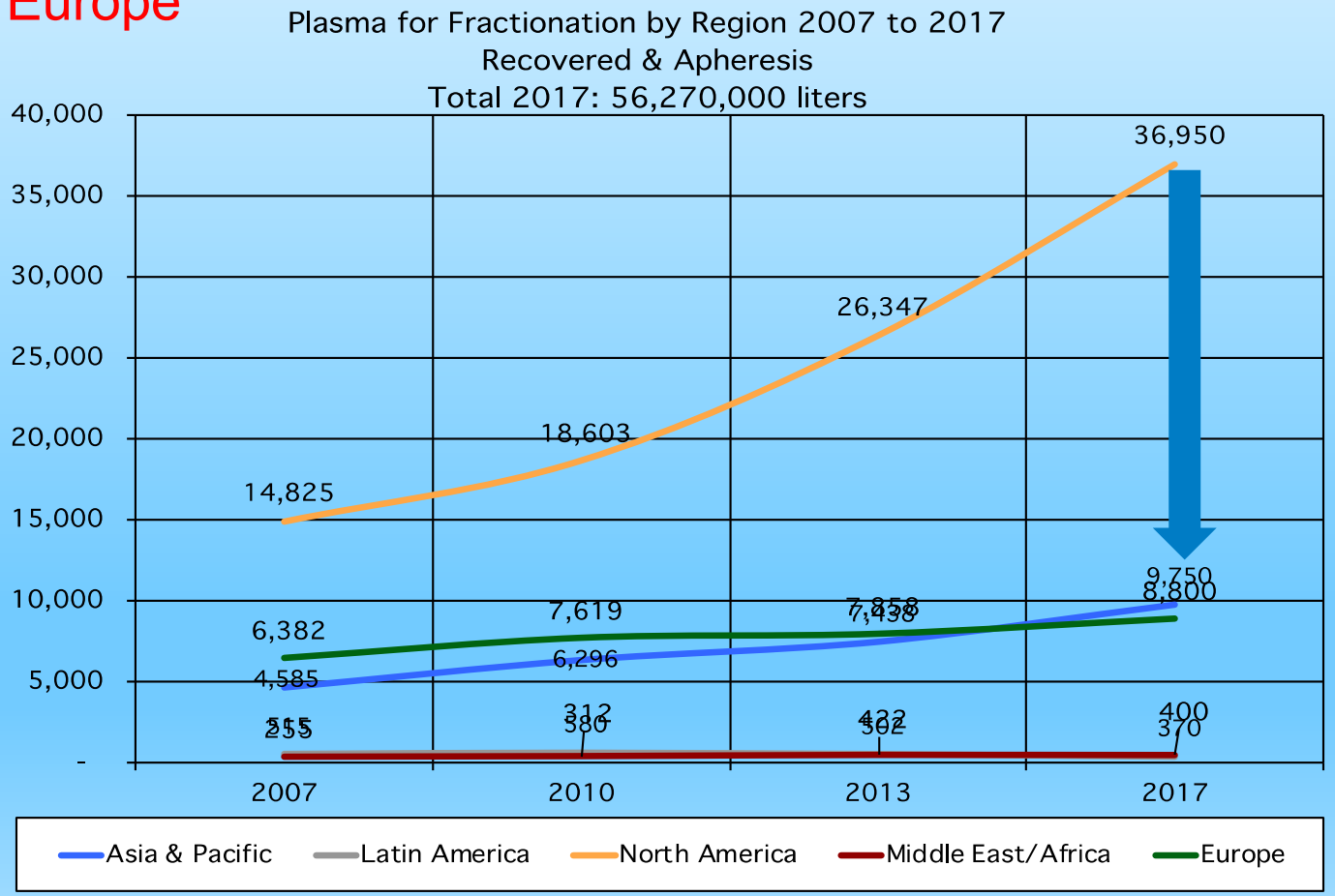
Blood collections have declined in all developed countries because of patient blood management (therefore the availability of RP as PfF has declined too)

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.*

RECOVERED PLASMA FOR FRACTIONATION

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

RECOVERED PLASMA FOR FRACTIONATION

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)

RECOVERED PLASMA FOR FRACTIONATION

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

CONCLUSIONS

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

Blutspendedienst
des Bayerischen Roten Kreuzes

Stand: 5/2014

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

ARBEITSGEMEINSCHAFT
PLASMAPHERESE E. V.

Plasmazentren finden ...

Ihr Standort Augsburg **Suchradius** 200 km **Suchen**

KEDPLASMA
Philippine Welser Str. 8
86150 Augsburg

0.2 km
Route

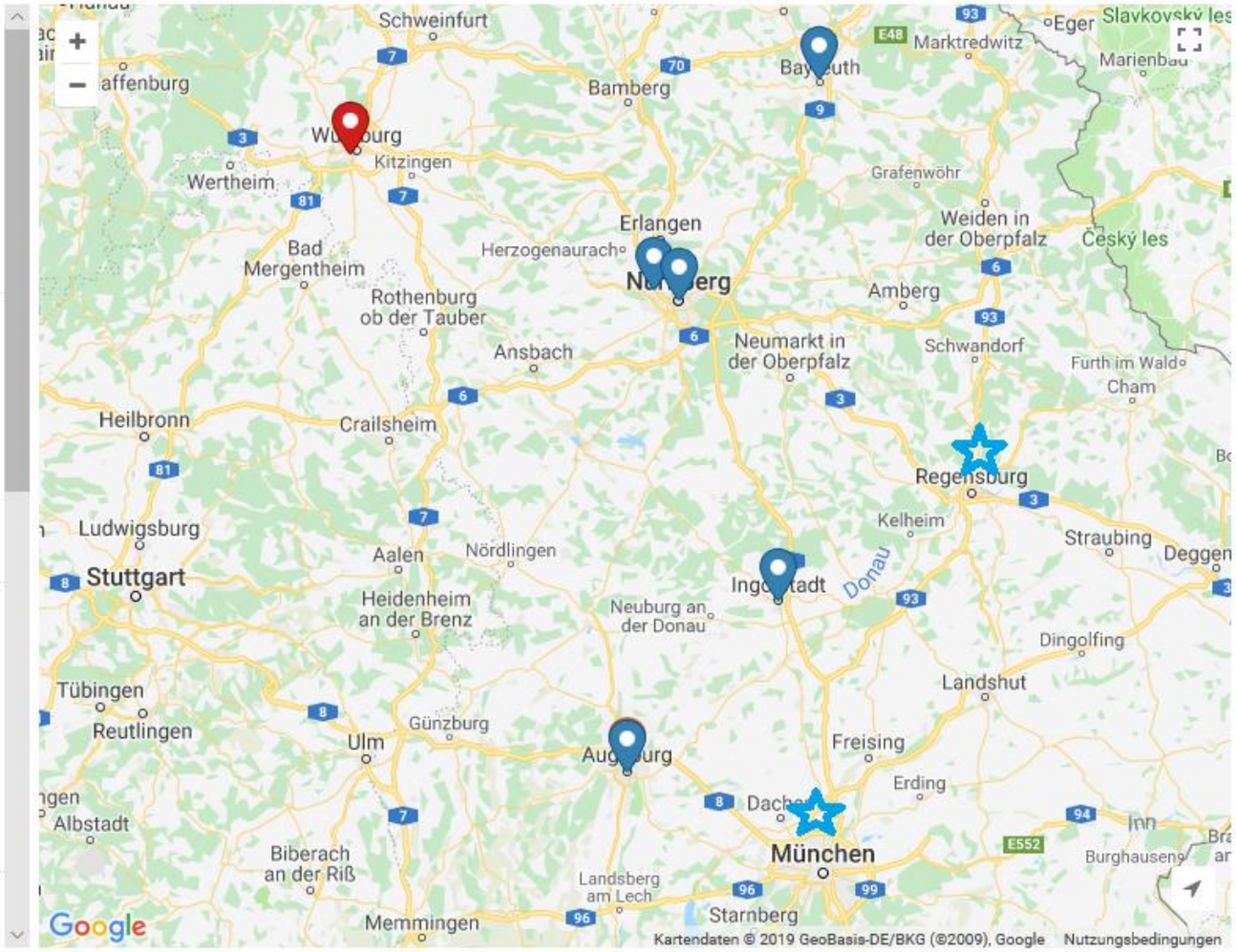
KEDPLASMA
Rathausplatz 11
85049 Ingolstadt

58.4 km
Route

CSL Plasma GmbH
Pfannenschmiedsgasse 5
90402 Nürnberg

120.8 km
Route

KEDPLASMA



DRK/BRK

staatlich kommunal

privat

Industrie

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.

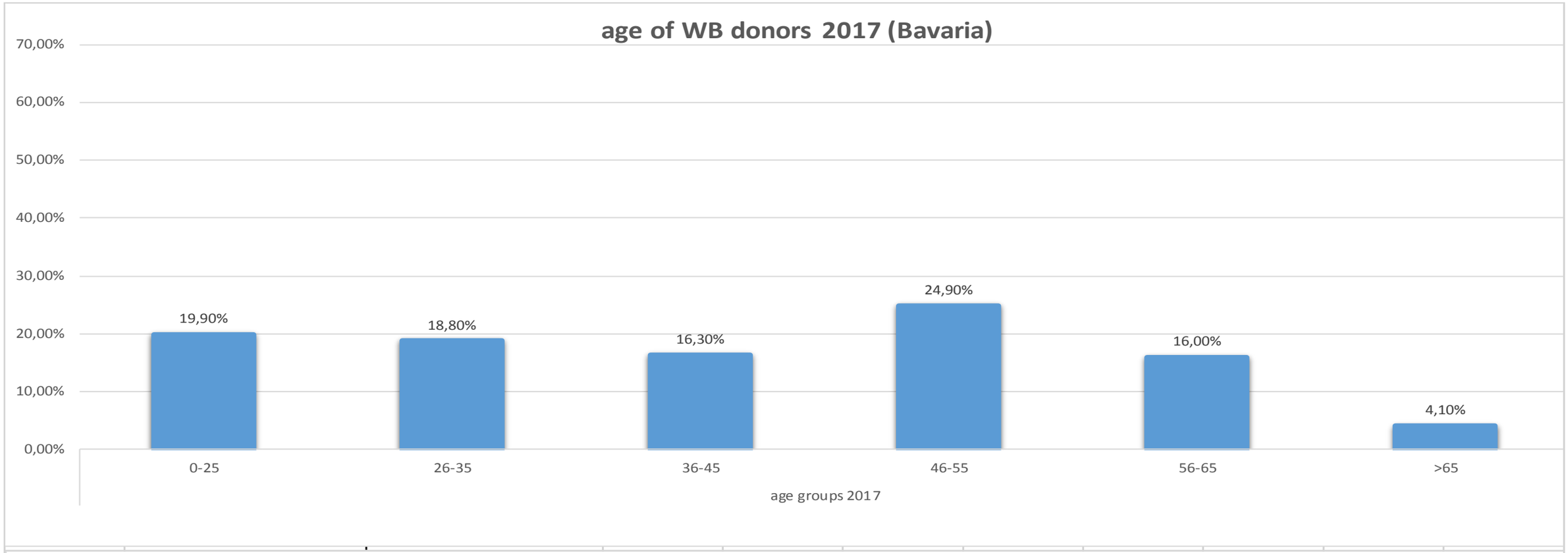
487,535
units of blood
were donated in Bavaria in 2017.

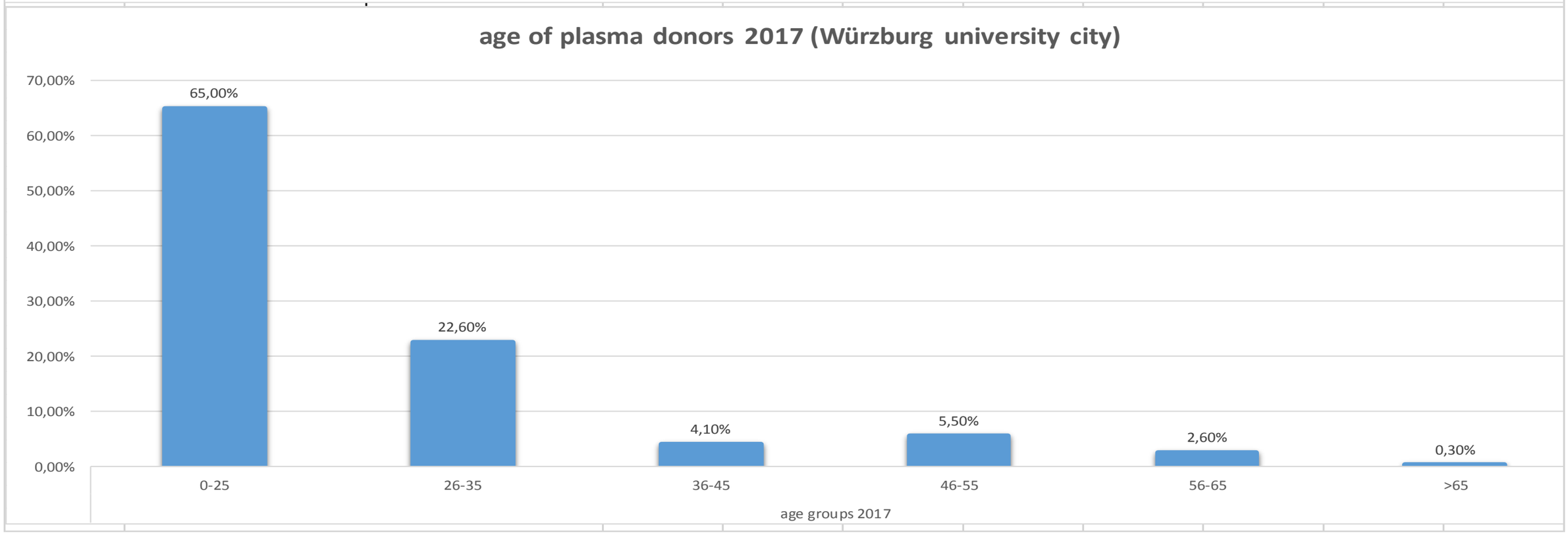
Ø 2
units of blood
on average were given by registered blood donors in 2017.

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

40 years
is the average age of a female person donating blood.

Blutspendedienst
des Bayerischen Roten Kreuzes


age of WB donors 2017 (Bavaria)
70,00%
60,00%
50,00%
40,00%
30,00%
20,00%
10,00%
0,00%
19,90%
18,80%
16,30%
24,90%
16,00%
4,10%
0-25
26-35
36-45
46-55
56-65
>65
age groups 2017


age of plasma donors 2017 (Würzburg university city)
70,00%
60,00%
50,00%
40,00%
30,00%
20,00%
10,00%
0,00%
65,00%
22,60%
4,10%
5,50%
2,60%
0,30%
0-25
26-35
36-45
46-55
56-65
>65
age groups 2017

Donation Frequency WB and Plasma at the BRK Blood Bank

Average number of donations per year (2017)

Whole blood donors*		Plasma donors **	
1	48,5 %	1 - 10	74,7 %
2	24,4 %	11 – 20	14,6 %
3	15,6 %	21 - 30	5,5 %
4	8,6 %	31 - 40	3,1 %
5	2,2 %	41-50	1,8 %
6	0,6 %	> 51	0,1 %

* 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)

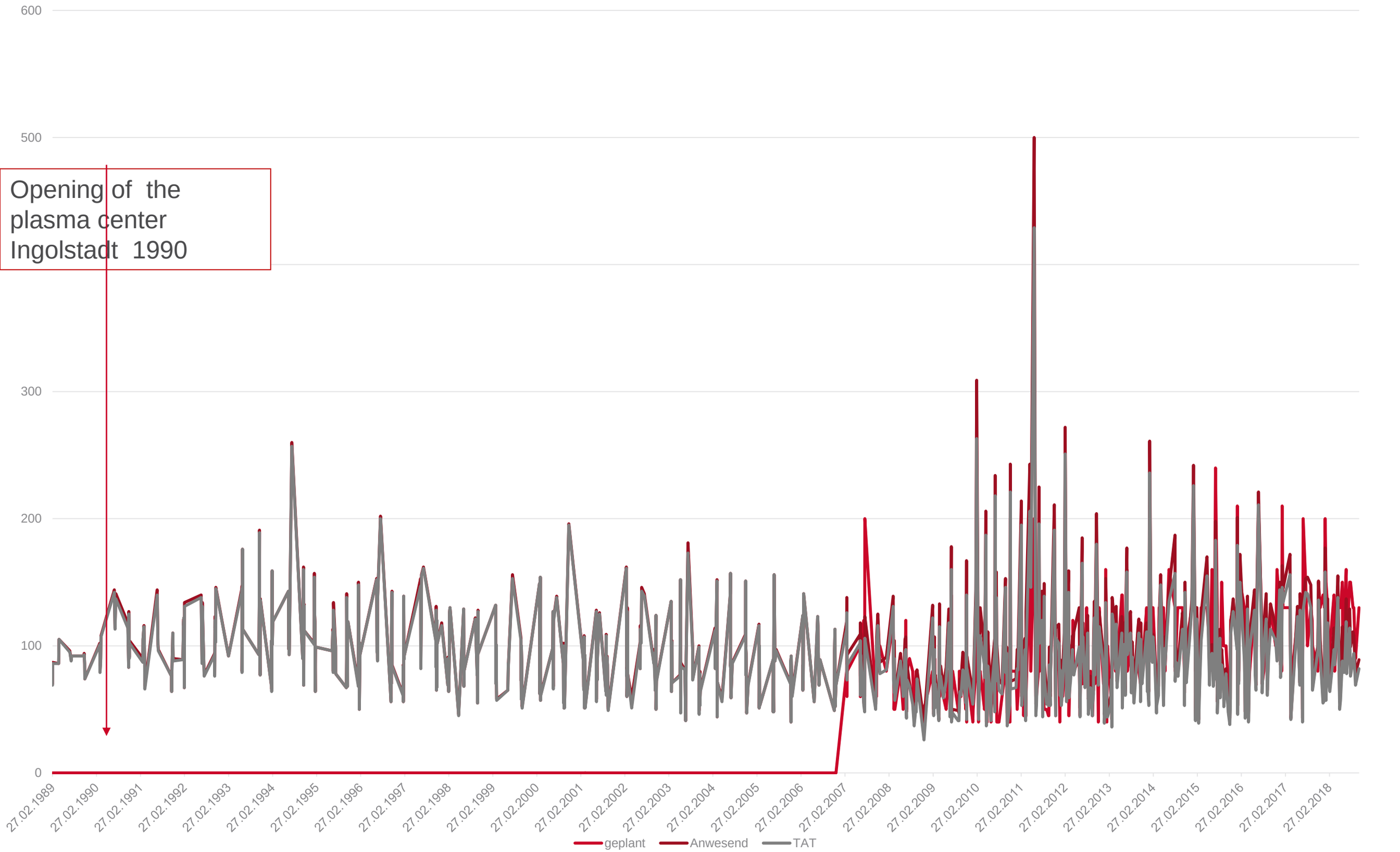
  „higher“ frequency of donation (10 / y)

Crowding out of whole blood donors to plasma??

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

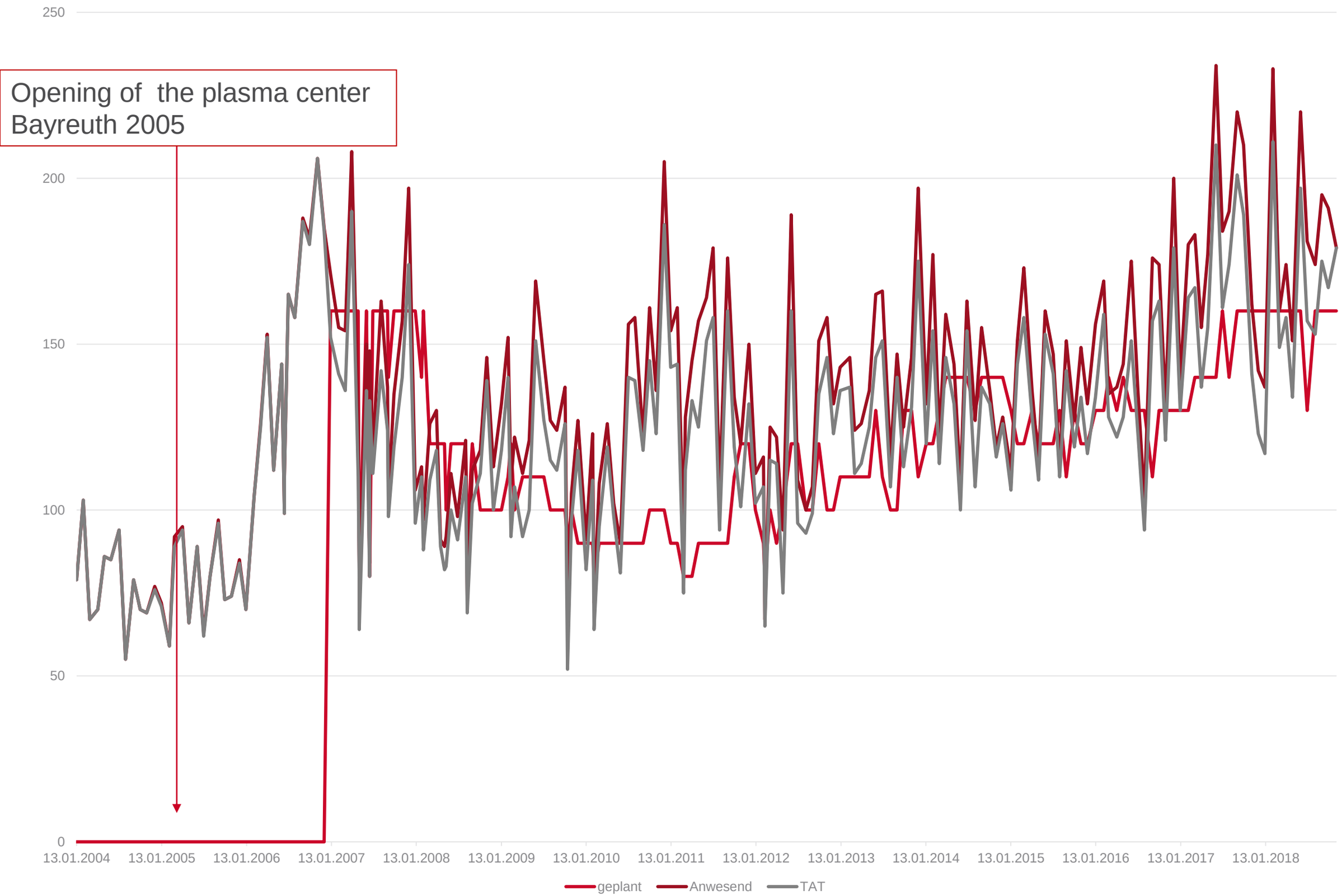
Figures after the opening of three plasma centers show no negative influence on WB donations in that particular area (no difference in the year before, compared to the years after opening)

Blood donation in the INGOLSTADT area 01/1989 until 10/2018



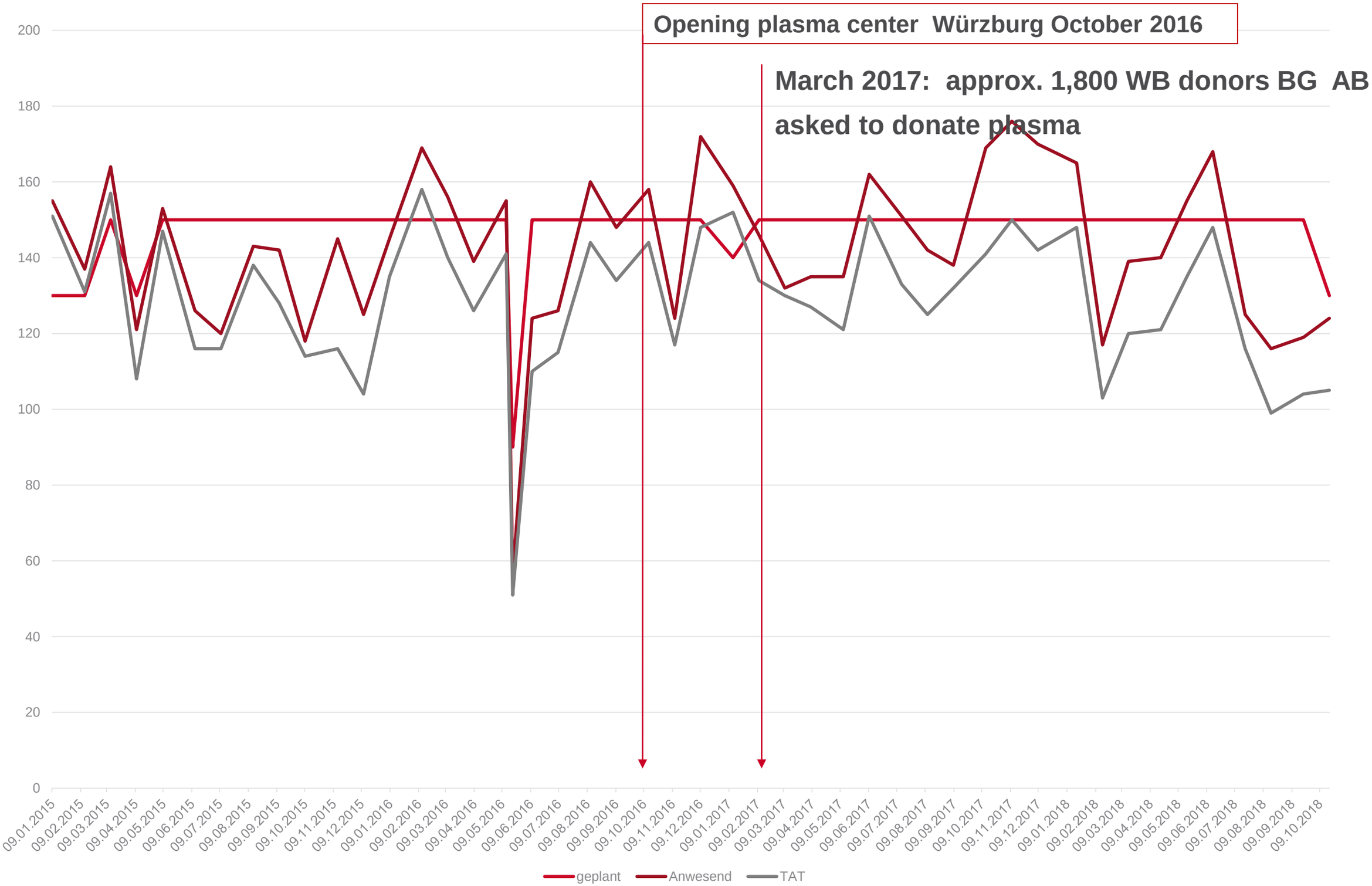
Blutspendedienst
des Bayerischen Roten Kreuzes

Blood donation in the city of Bayreuth 01/2004 until 11/2018



Blutspendedienst
des Bayerischen Roten Kreuzes

Blood donation in the city of Würzburg 01/2015 until 10/2018



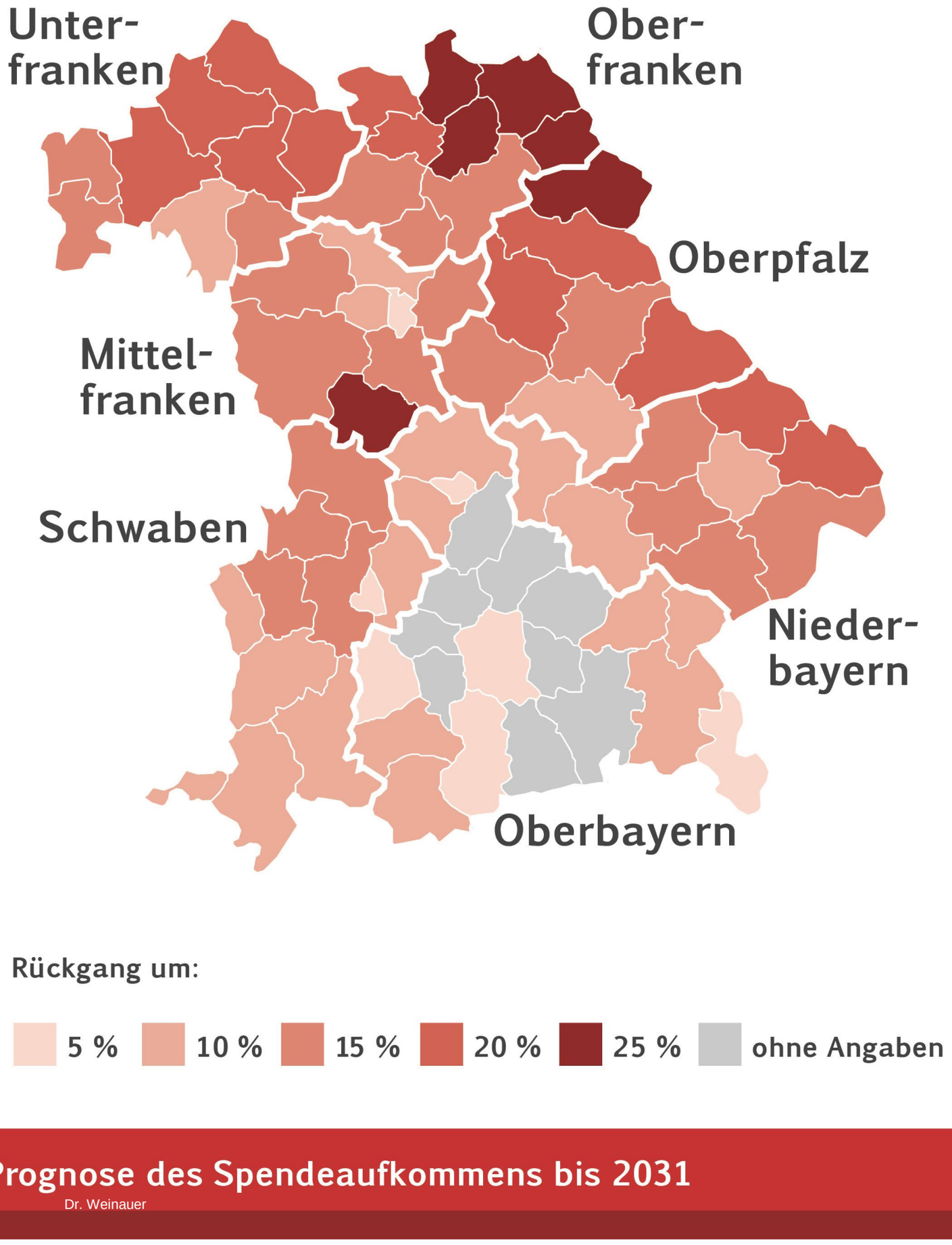
Blutspendedienst
des Bayerischen Roten Kreuzes

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**



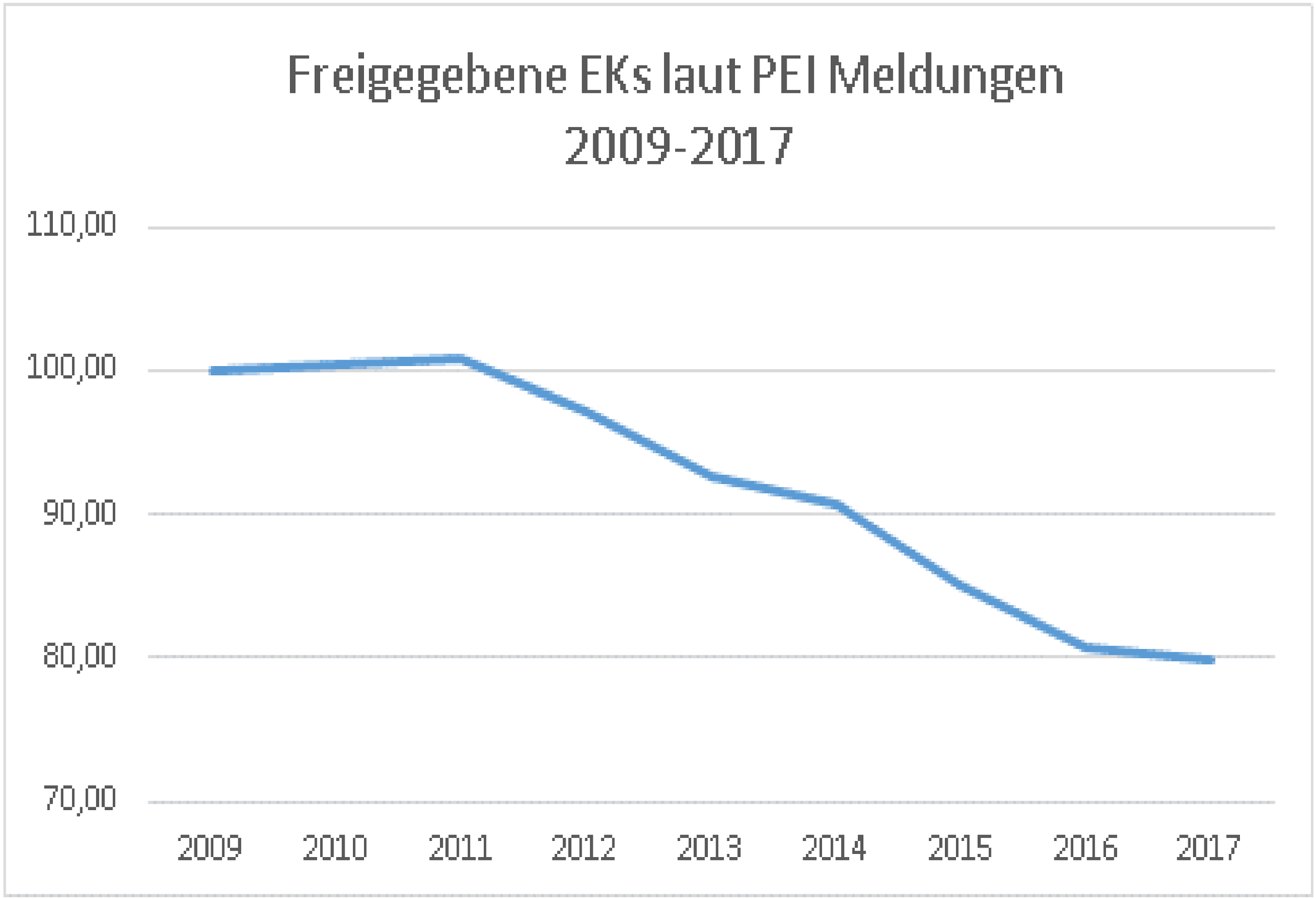
Prognose des Spendeaufkommens bis 2031

Dr. Weinauer

Blutspendedienst
des Bayerischen Roten Kreuzes

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)

PLASMA FOR FRACTIONATION BY COUNTRY
SOURCE & RECOVERED
FROM 2000 TO 2017
(Liters x 000)

	2017		
	Recovered	Apheresis	Total
Austria	100	555	655
Belgium	120	-	120
Bulgaria	15	-	15
Croatia	25	-	25
Czech Republic	60	421	481
Denmark	44	39	83
Estonia	11	-	11
Finland	42	-	42
France	632	260	892
Germany	985	1.977	2.962
Greece	2	-	2
Hungary	79	323	402
Italy	620	210	830
Latvia	8	-	8
Lithuania	11	3	14
Netherlands	92	234	327
Norway	54	10	64
Poland	229	84	314
Portugal	90	-	90
Serbia	10	-	10
Slovakia	20	-	20
Slovenia	11	-	11
Spain	353	20	373
Sweden	98	25	123
Switzerland	70	5	75
Other Europe	30	-	30
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

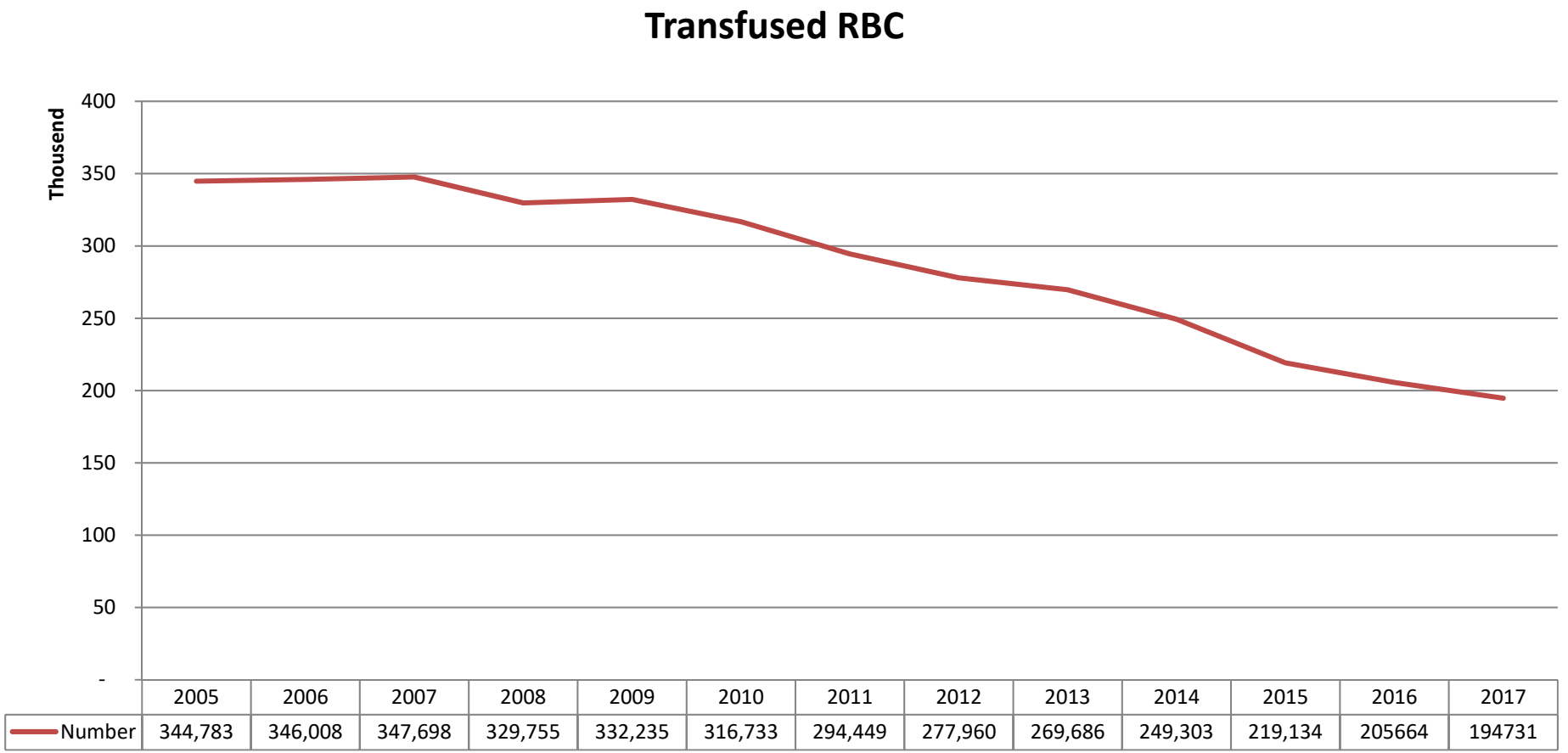
Obstacles to Independence of Plasma for Fractionation in Europe

- 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
- IVIG & albumin national self-sufficiency (2010)

Then There Was a Decrease….

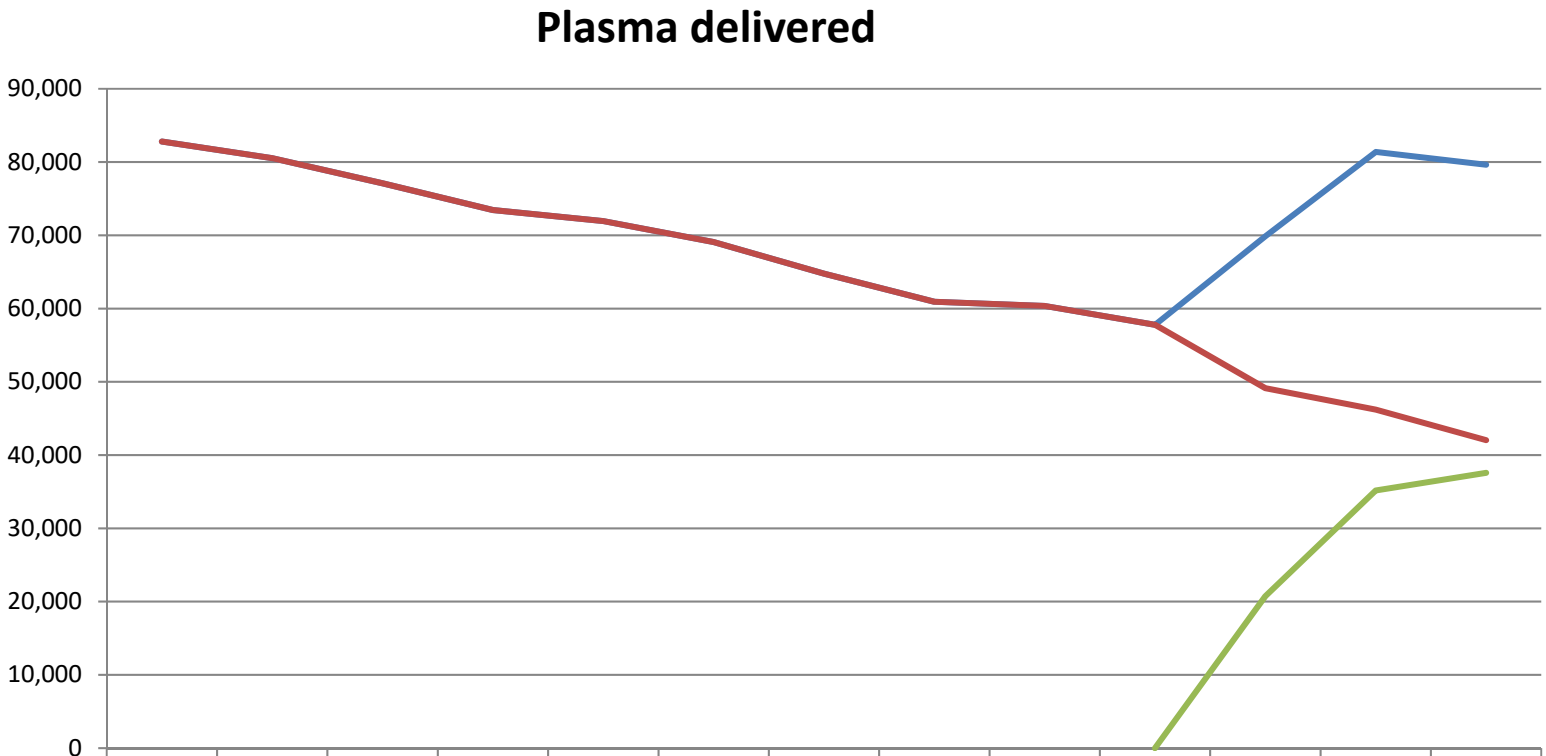


	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017
Number	344,783	346,008	347,698	329,755	332,235	316,733	294,449	277,960	269,686	249,303	219,134	205664	194731

Mind the Gap…

- In 2013 decision by the health authorities to produce plasma by plasmapheresis to fulfill the contract

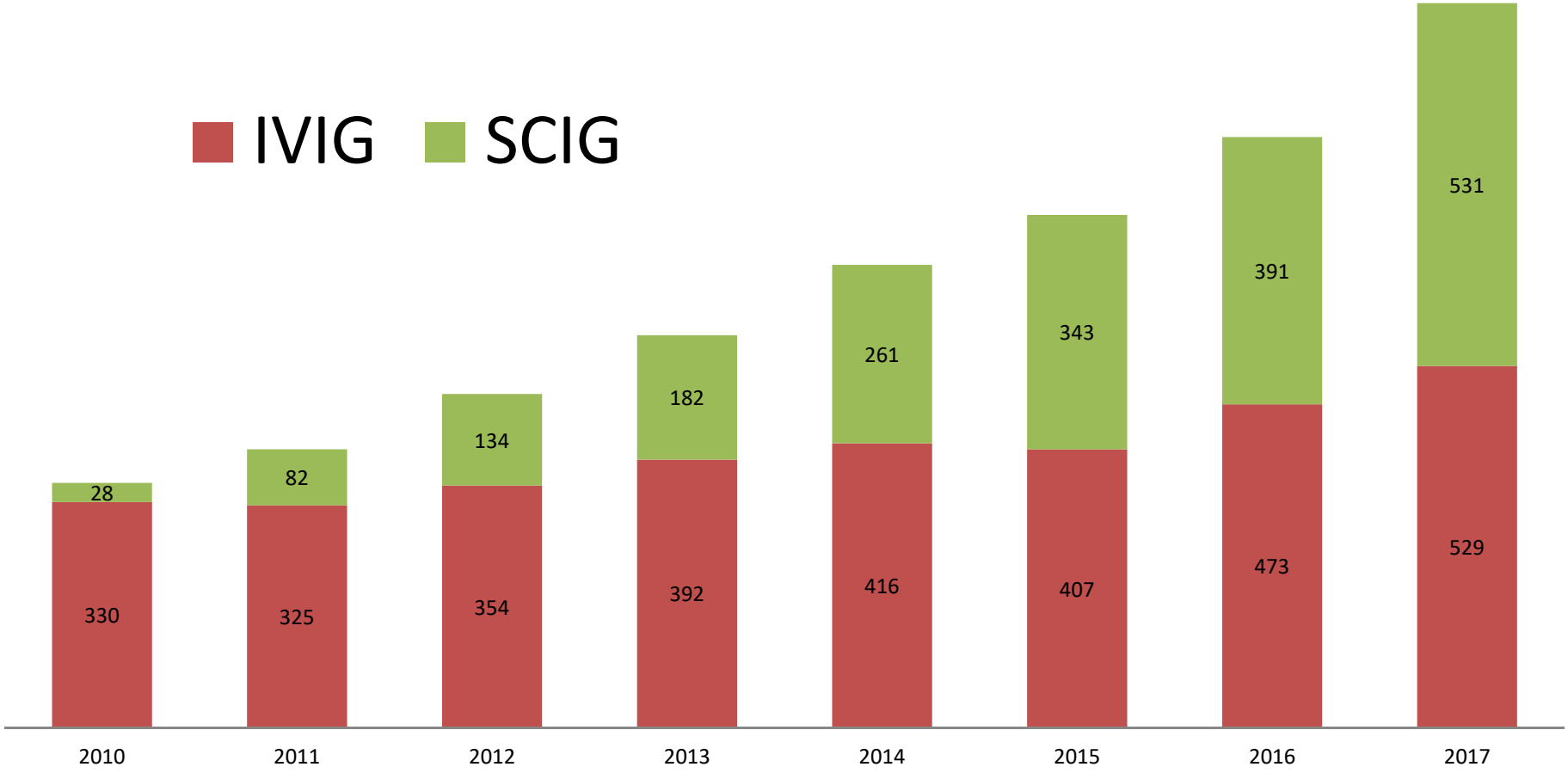
Plasma Delivered



	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017
Kg Total	82,790	80,532	77,102	73,444	71,933	69,074	64,761	60,931	60,369	57,776	69,865	81,384	79,625
Kg Recovered	82,790	80,532	77,102	73,444	71,933	69,074	64,761	60,931	60,369	57,776	49,126	46,210	42,040
Kg Source										0	20,739	35,174	37,585

Then There Was an Increase…

Use of IG in Denmark; pop. 5.8 mio.

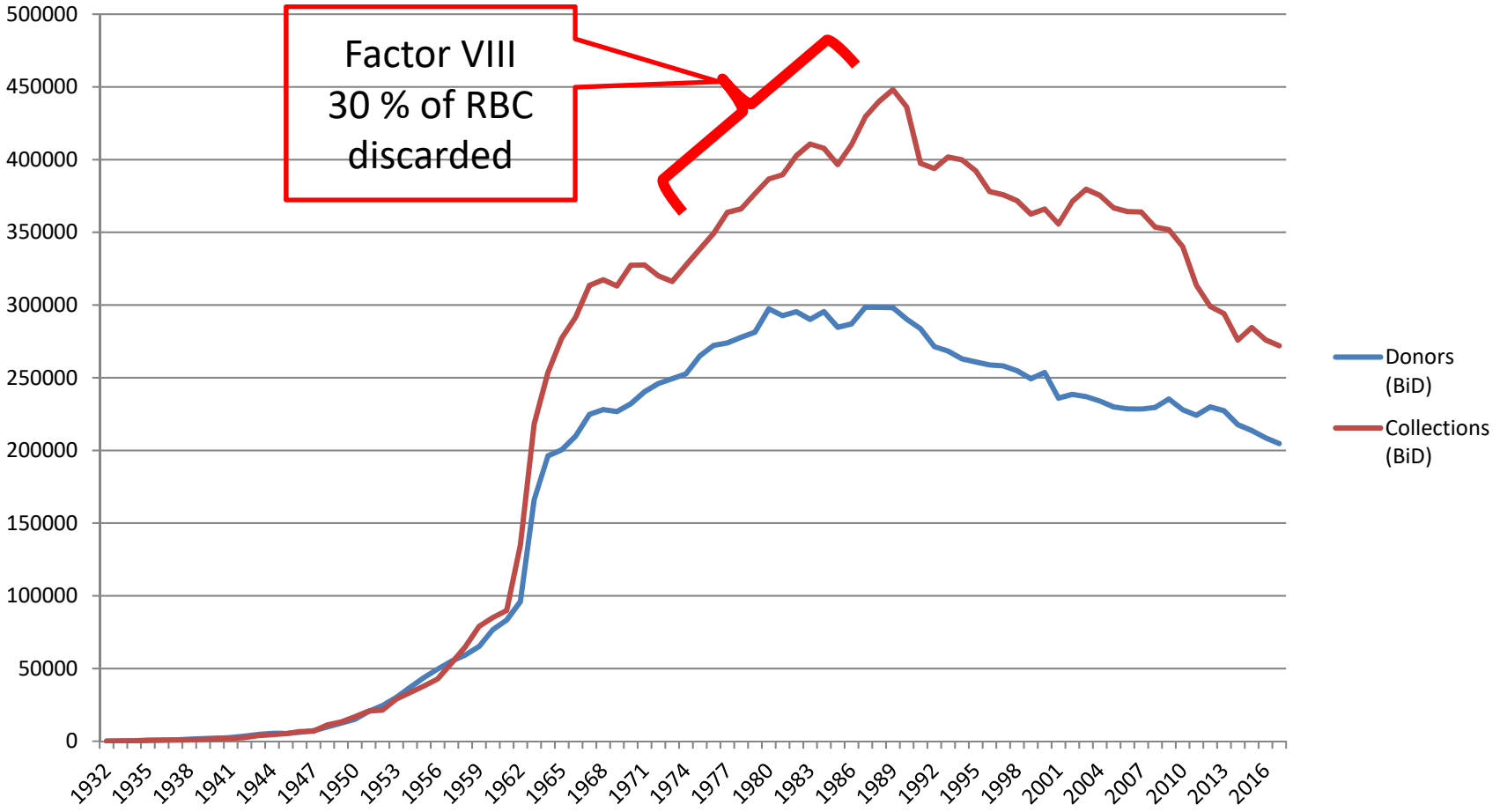


…and an Even Bigger Gap!

- 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?



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

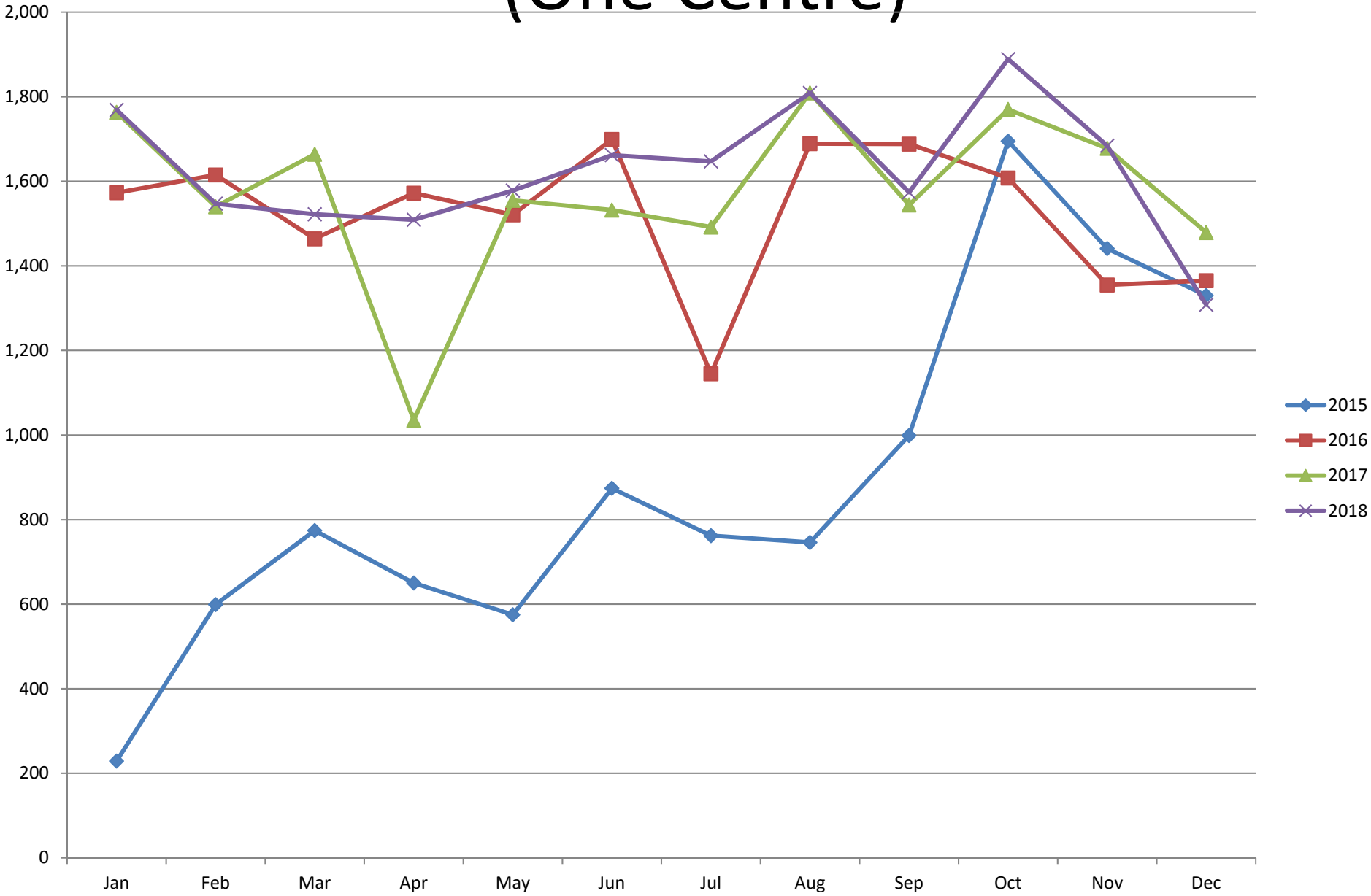
- 60-70 kg: 600 ml
- 70-80 kg: 700 ml
- > 80 kg and male: 800 ml

- 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

Number of Plasmapheresis Collections (One Centre)



Results in Numbers (One Centre)

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

- 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

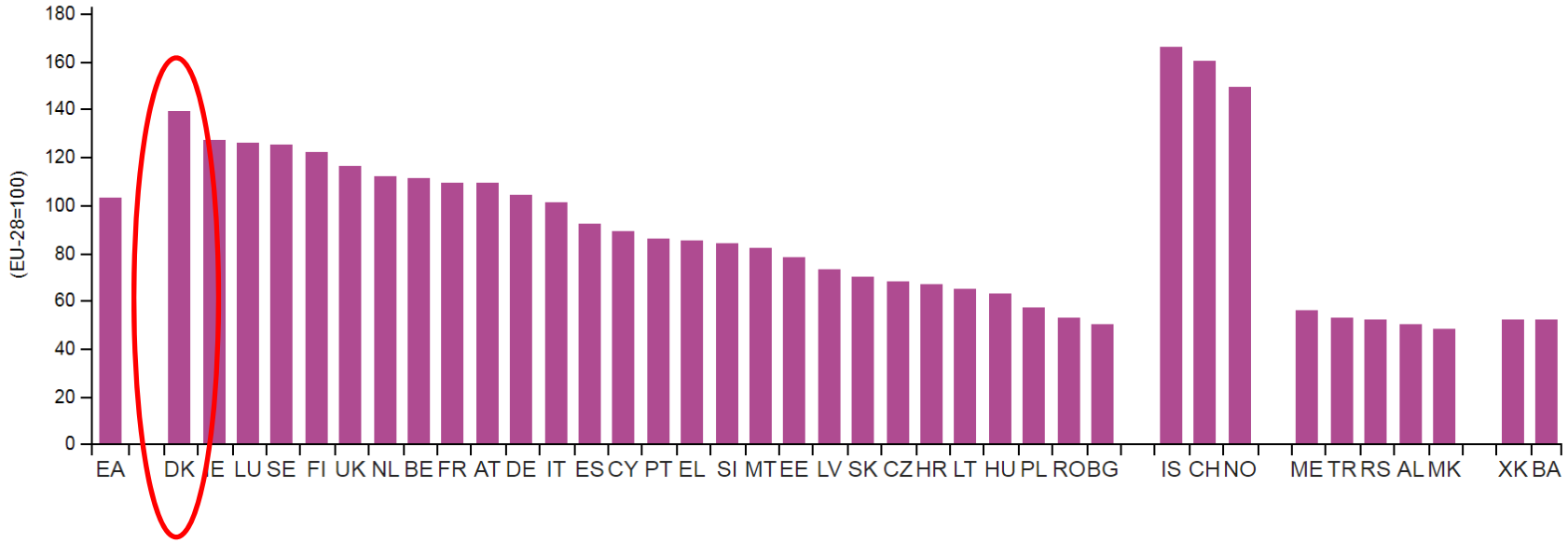
- Productivity per hour 
- Production per FTE 
  - Working hours per week 34.5 hours
  - Holidays and public holidays 6 weeks + 10 days
- Production and cost per FTE 
- General level of costs 

Comparative price levels of cons

https://ec.europa.eu/eurostat/statistics-explained/index.php/Comparative_price_levels_of_consumer_goods_and_services

Tweet 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



XK : This designation is without prejudice to positions on status, and is in line with UNSCR 1244 and the ICJ Opinion on the Kosovo Declaration of Independence.

Source: Eurostat (online data code: prcpppind)

eurostat

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

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- 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
- Change of operation model
  - Blood Establishments
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  - Number of hours work per week and year
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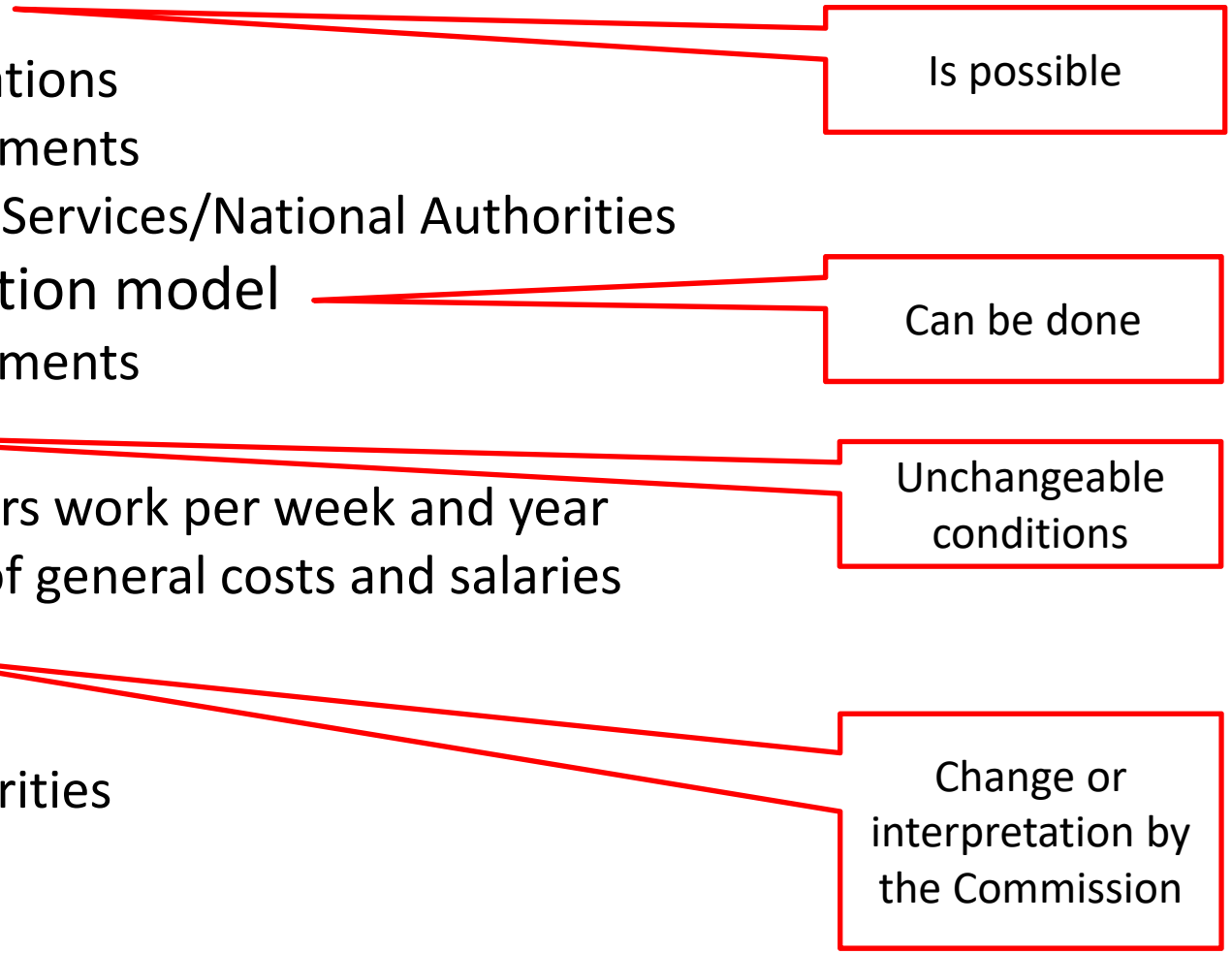
  - National Authorities



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

Contents

- 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

*excluding anticoagulant

	Germany 2017	Europe 2017	USA since 1992
Maximum per donation, ml	50 - 60 kg 650 60 - 70 kg 750 70 kg 850	750*	50 – 67 kg 690 ml 68 – 79 kg 825 ml >79 kg 880 ml
Donation frequency Maximum per year	Twice weekly 60	Twice weekly 33	Twice weekly 104
Minimum IgG, g/l	6.0 Every 5th donation	6.0 At least annually	Serum electrophoresis every 4 months
Minimum total protein, g/l	60 Every 5th donation	60 At least annually	60 Every 4 months
Hemoglobin, g/l	♀ 120, ♂ 135	♀ 125, ♂ 135	125

Early clinical studies

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.

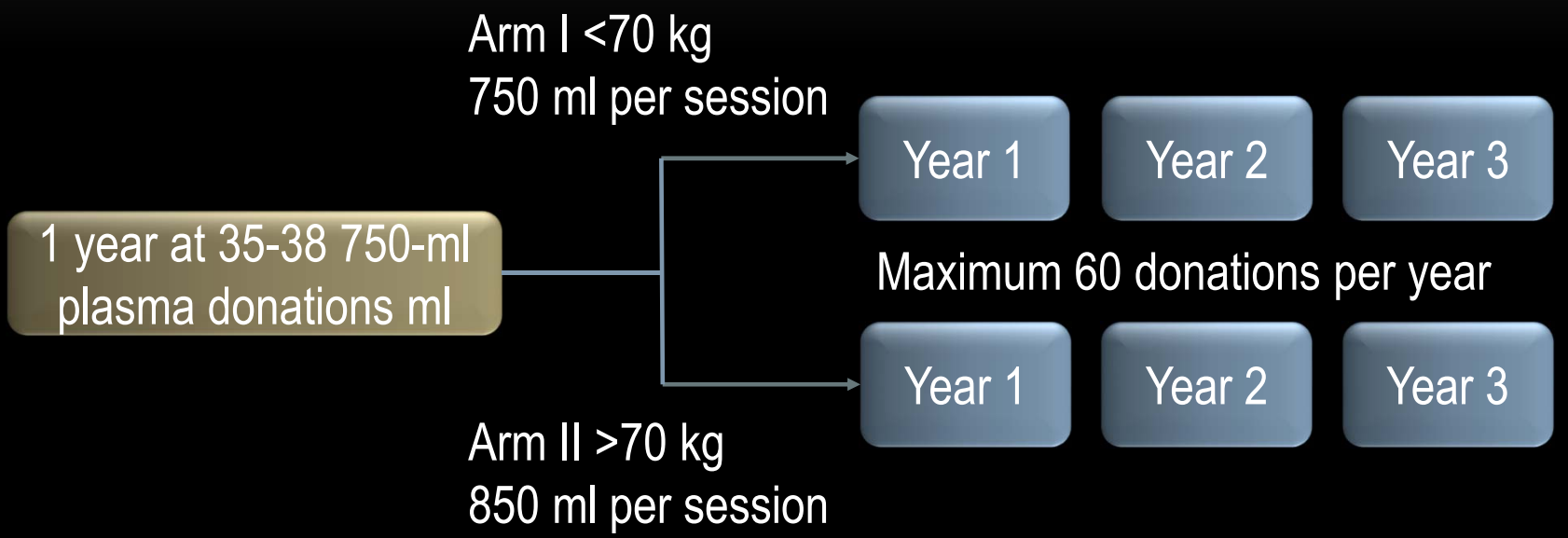
Study on intensified plasmapheresis (SIPLA)

Prospective identification of dropout reasons

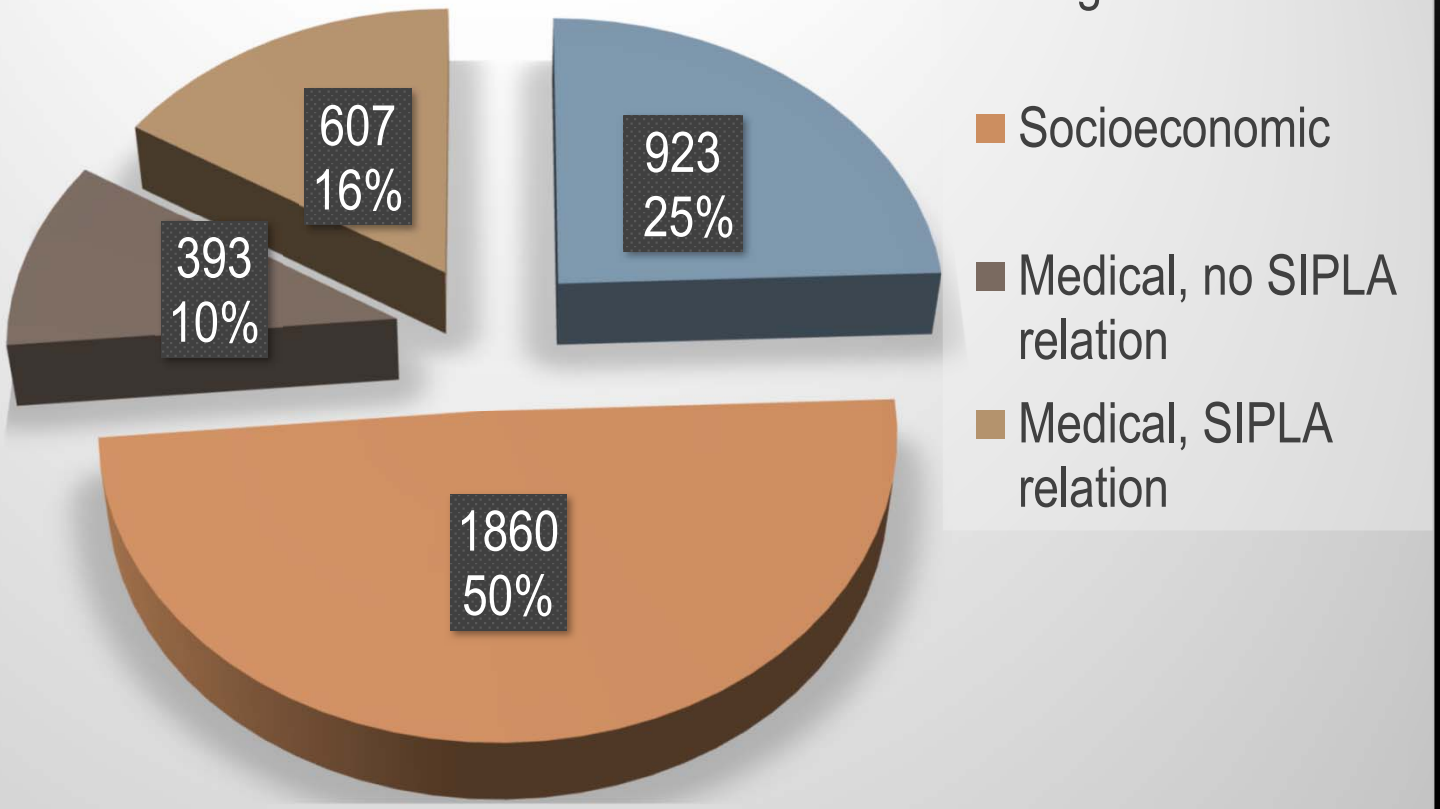
Is intensified plasma donation safe?

- 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

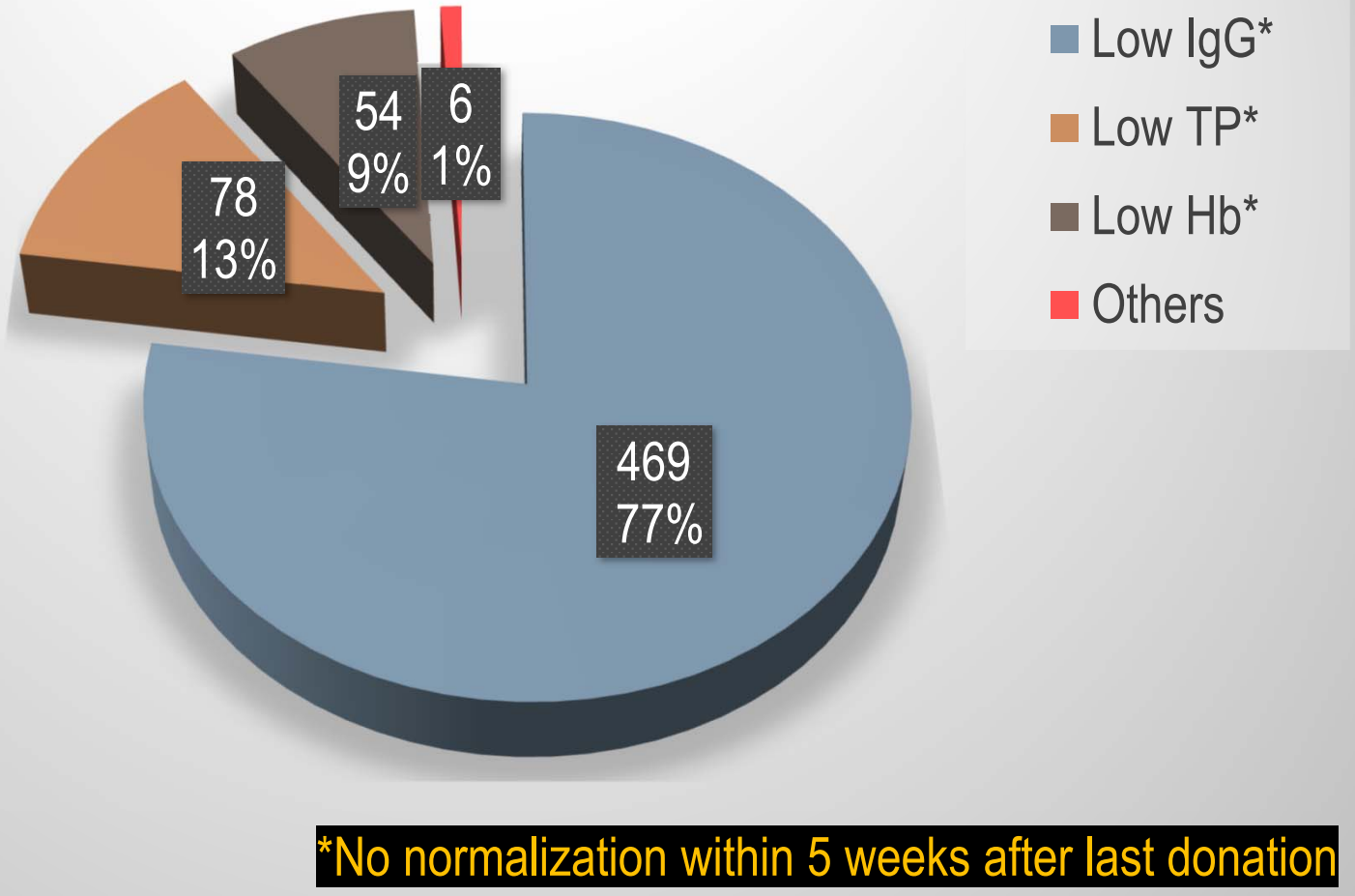
Study on intensified plasmapheresis (SIPLA)



SIPLA outcome after 3 years



Dropouts for SIPLA-related medical reasons



*No normalization within 5 weeks after last donation

SIPLA - risks for dropping out related to plasma donation

Variable	Hazard ratio	P-value
Higher initial IgG	**0.1** (0.0-0.2)	<0.0001
Age, per 10 years	**0.8** (0.7-0.9)	<0.0001
Male sex	**0.6** (0.5-0.7)	<0.0001
Days between 2 donations	**0.5** (0.4-0.6)	<0.0001
Body weight, per 10 kg	1.0 (0.9-1.1)	n.s.
Higher initial total protein	1.1 (0.9-1.4)	n.s.
Higher initial Hb	0.8 (0.6-1.2)	n.s.
ml plasma/kg b.w./session	1.4 (1.0-2.1)	n.s.

Main differences between SIPLA and SIPLA II

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

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

	Conditions	Donations	Total, %	Severe, %
Kiessig S 2013, prospective	SIPLA II	70,000	0.22	0.09
Diekamp U 2014, retrospective	Germany 2010	1,107,846	0.51	0.03

Why IgG ≥ 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

Orange JS, Clin Immunol 2010;137:21–30

IgG replacement, minimum IgG trough target level 5 g/l, better > 6.0 g/l or greater

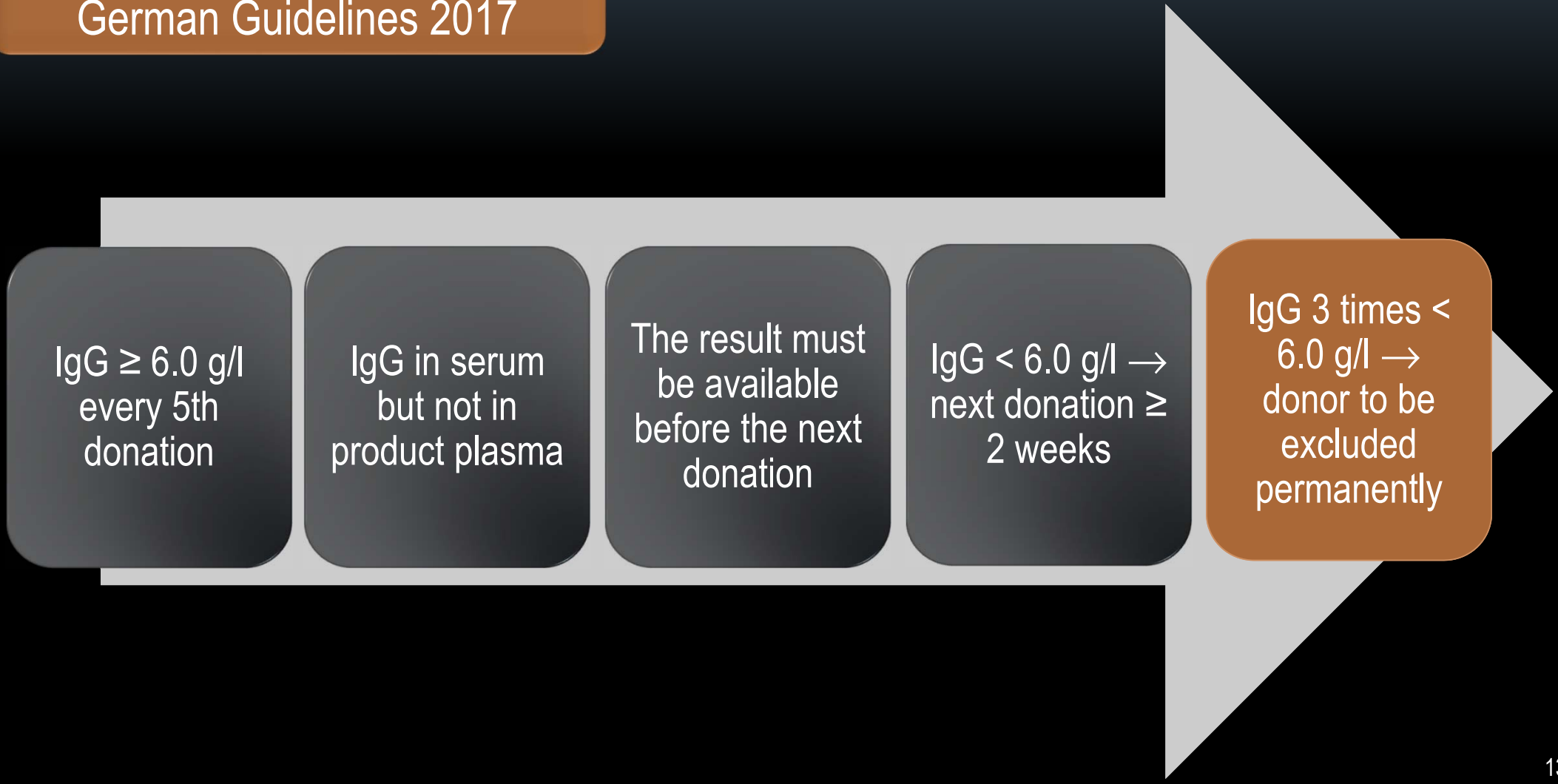
IgG levels < 6 g/l in plasma donations according to the 2010 German Guidelines
Möller Anke, Dissertation 2014

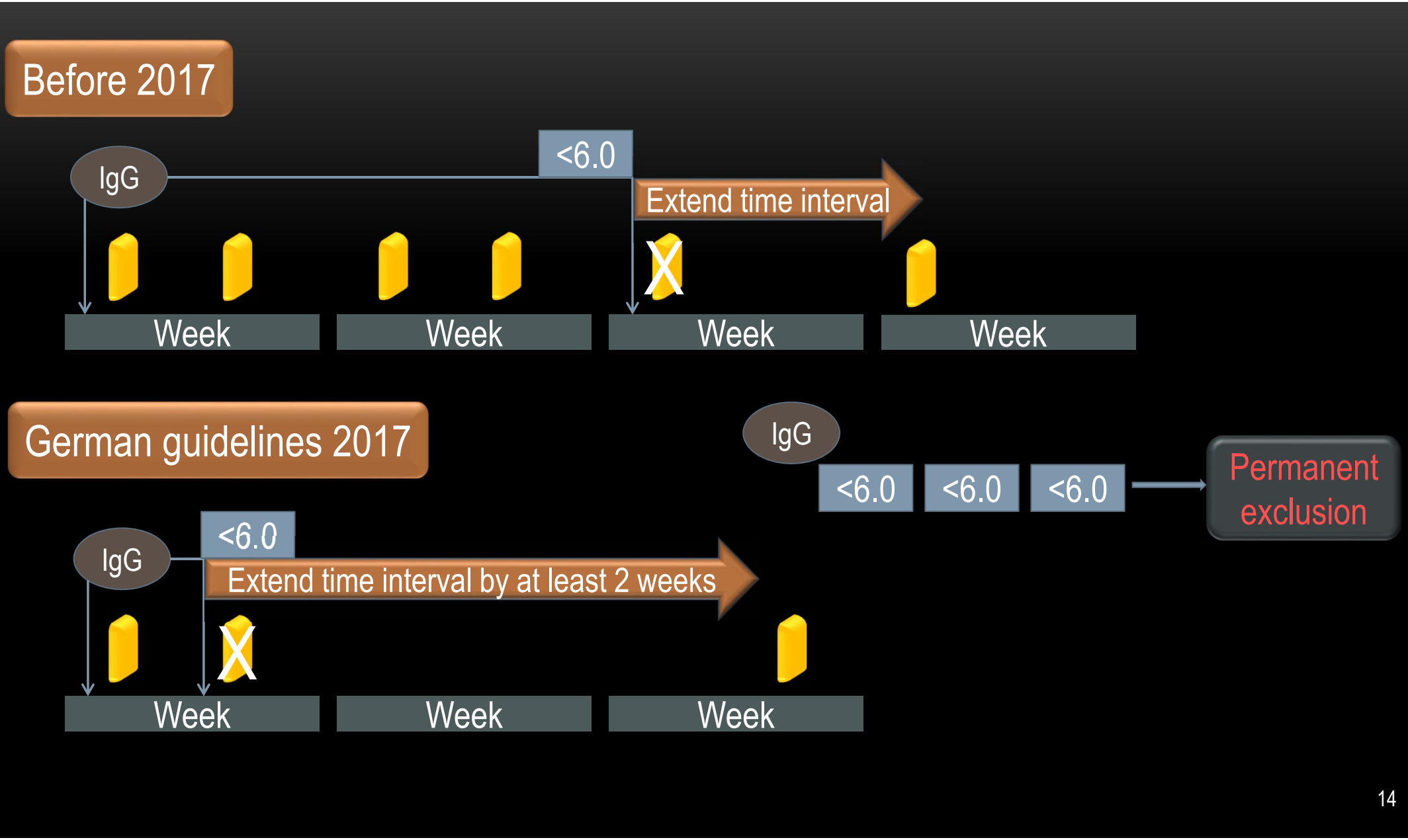
1293 donations with IgG < 6 g/l

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%

Donor safety – IgG
German Guidelines 2017




Before 2017
IgG
<6.0
Extend time interval
Week
Week
Week
Week
German guidelines 2017
IgG
<6.0
<6.0
<6.0
Permanent exclusion
IgG
<6.0
Extend time interval by at least 2 weeks
Week
Week
Week

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.

IgG serum/IgG PP	IgG determined in PP g/l	Calculated serum IgG g/l
1.1	5.4	6.0
1.32	4.5	6.0

Why donation volumes including citrate?

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

	Ratio IgM serum/IgM PP	Volume excluding citrate, ml	Volume including citrate, ml
Center 1	1.09	650	700
Center 2	1.27	650	825

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
  Fischer T et al. Transfus Apheresis Sci 2013;49:80
- 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

Conclusions

IgG depletion limits the intensity of plasma donation
→ individual donation intervals

Close monitoring

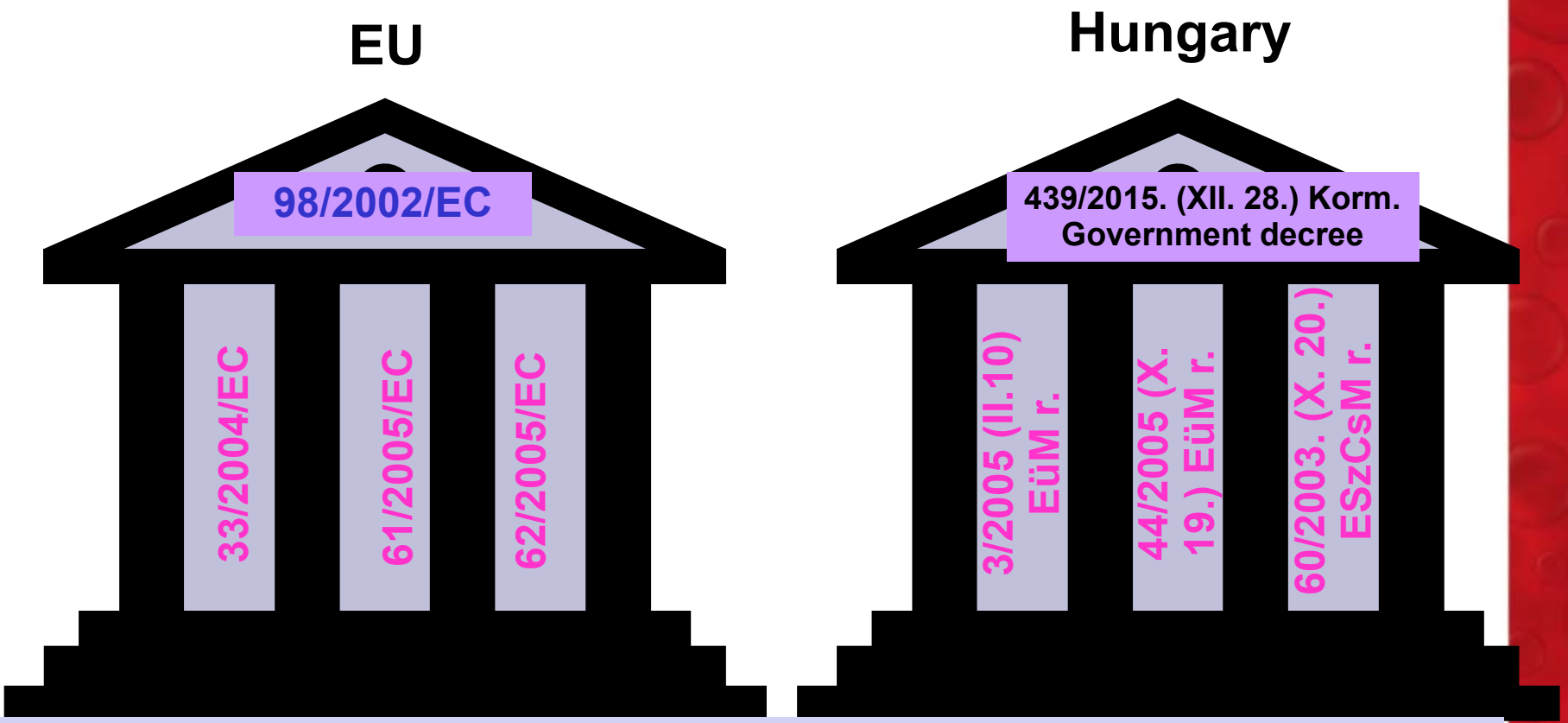
- Every 5th donation
- Lower limit of the reference range → 6.0 g/l
- Determination in serum, not in product plasma
- Results have to be available before the next donation
- IgG below 6 g/l → prolong donation interval
- IgG below 6 g/l 3 times → permanent exclusion from plasma donation


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,
Strasbourg, 29-30 January, 2019.

Hungarian regulation on blood supply



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 Transfsusion 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.).

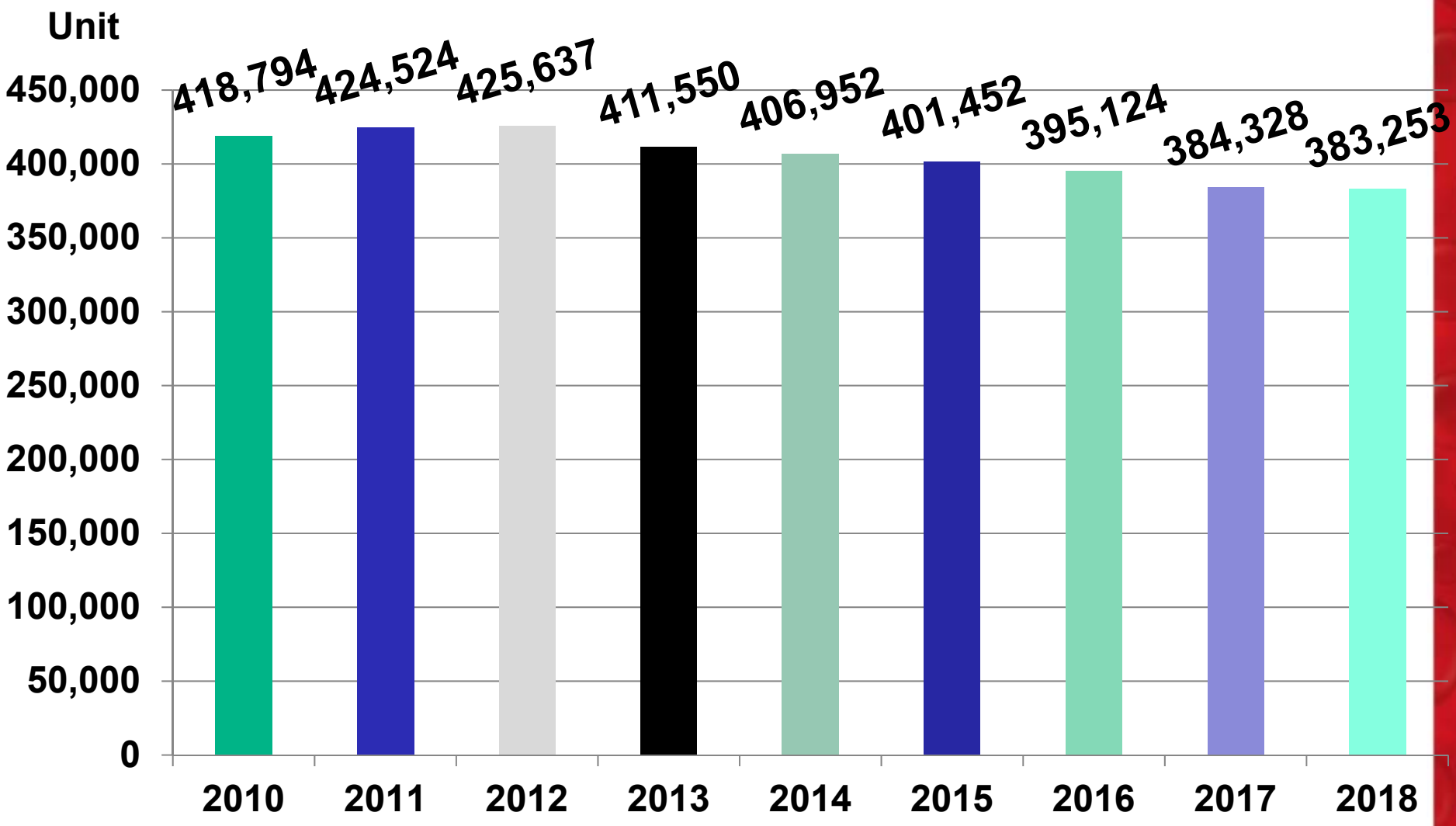
To prevent the TTI.

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

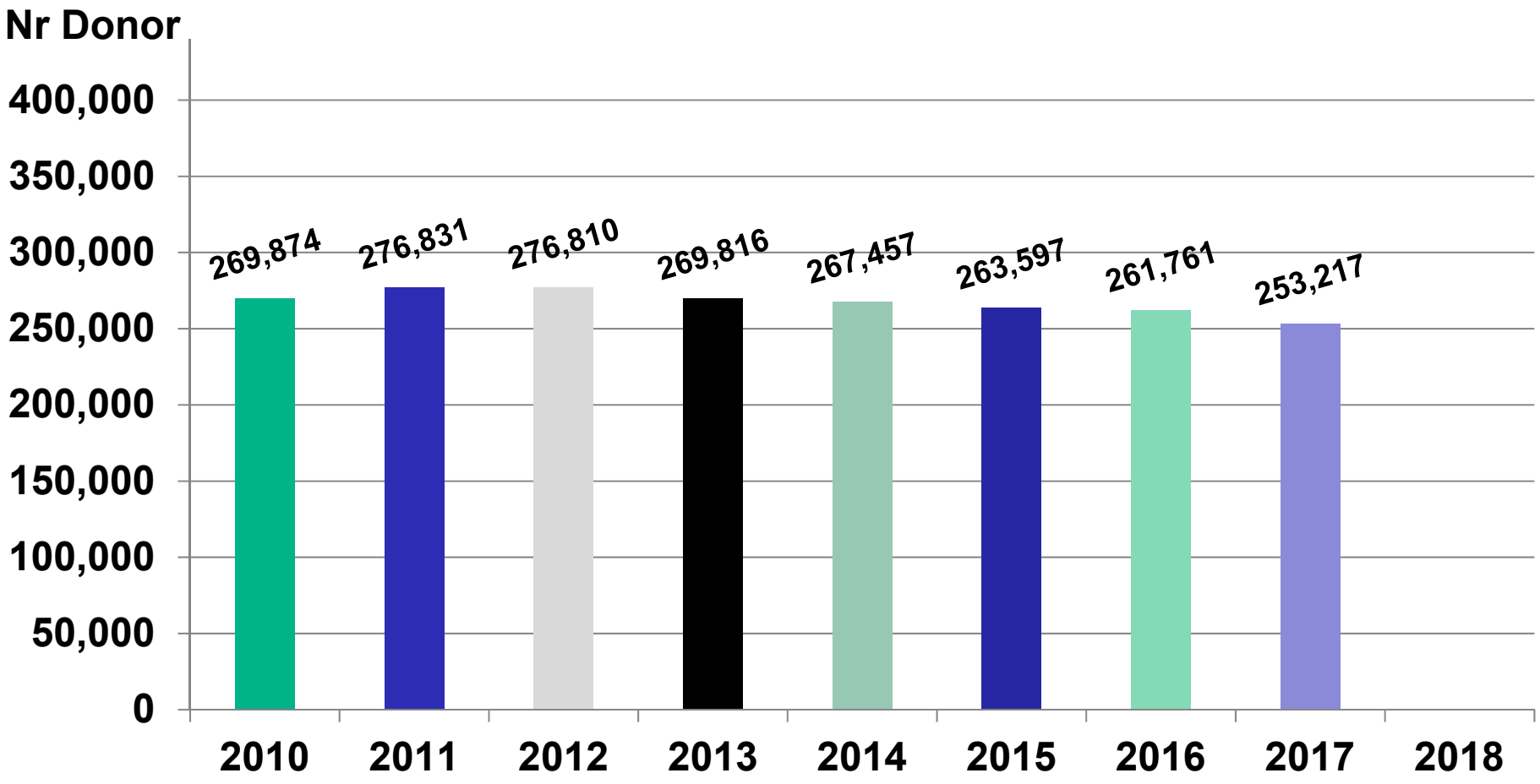
Every 6 month they should send their procedure's data (it is confidential), but their donor deferral riports are implemented into the *e*Progesa, unique donor register to improve the blood safety.

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

Collected Whole blood



Whole blood donors



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

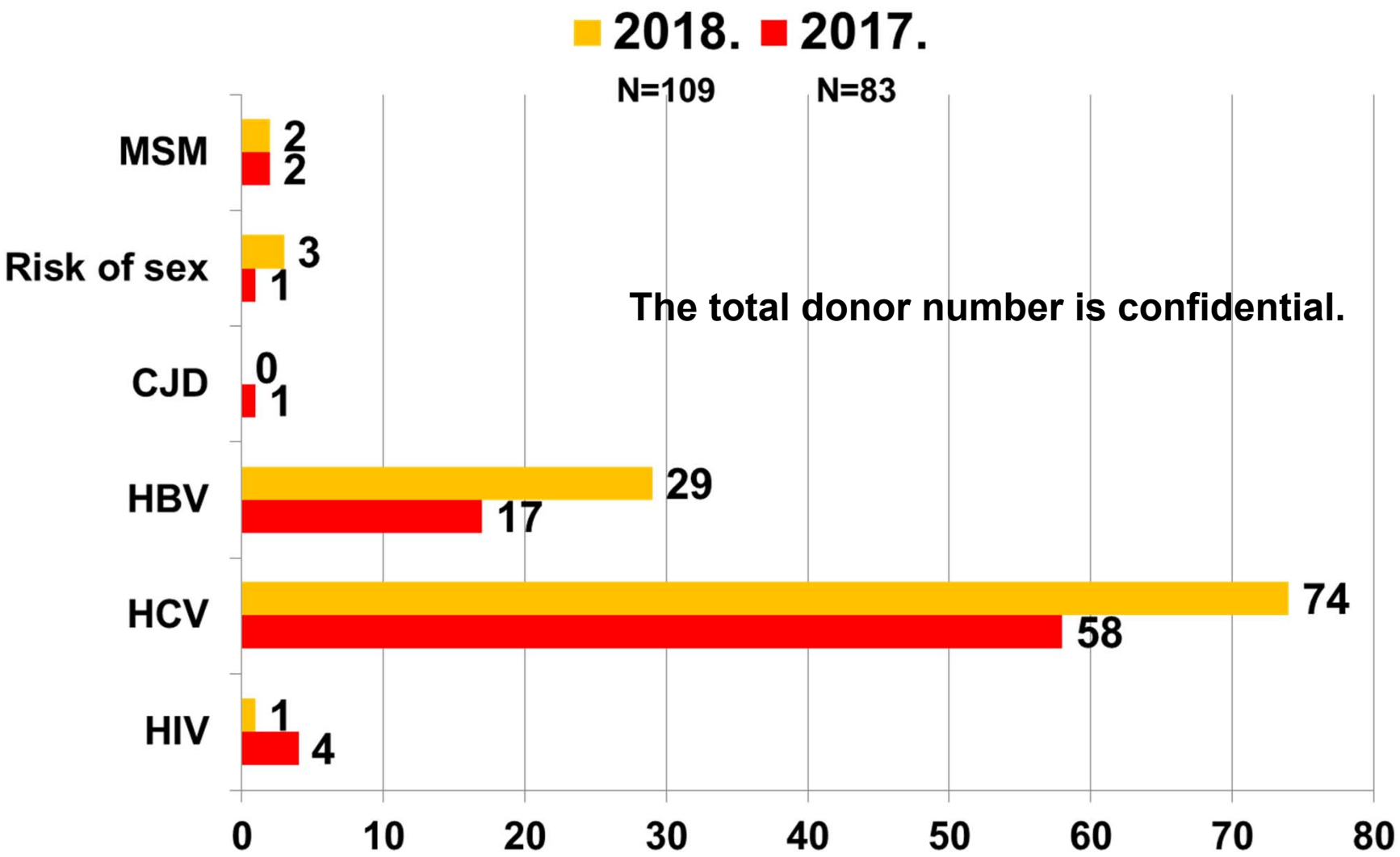
- **Number of Health Insurance, this a key ID Nr**
- **Date of birth,**
- **Gender,**

Communication through

- **website**
- **API (*application programming interface) or* web service**

Post Donation Information from the plasmapheresis centres

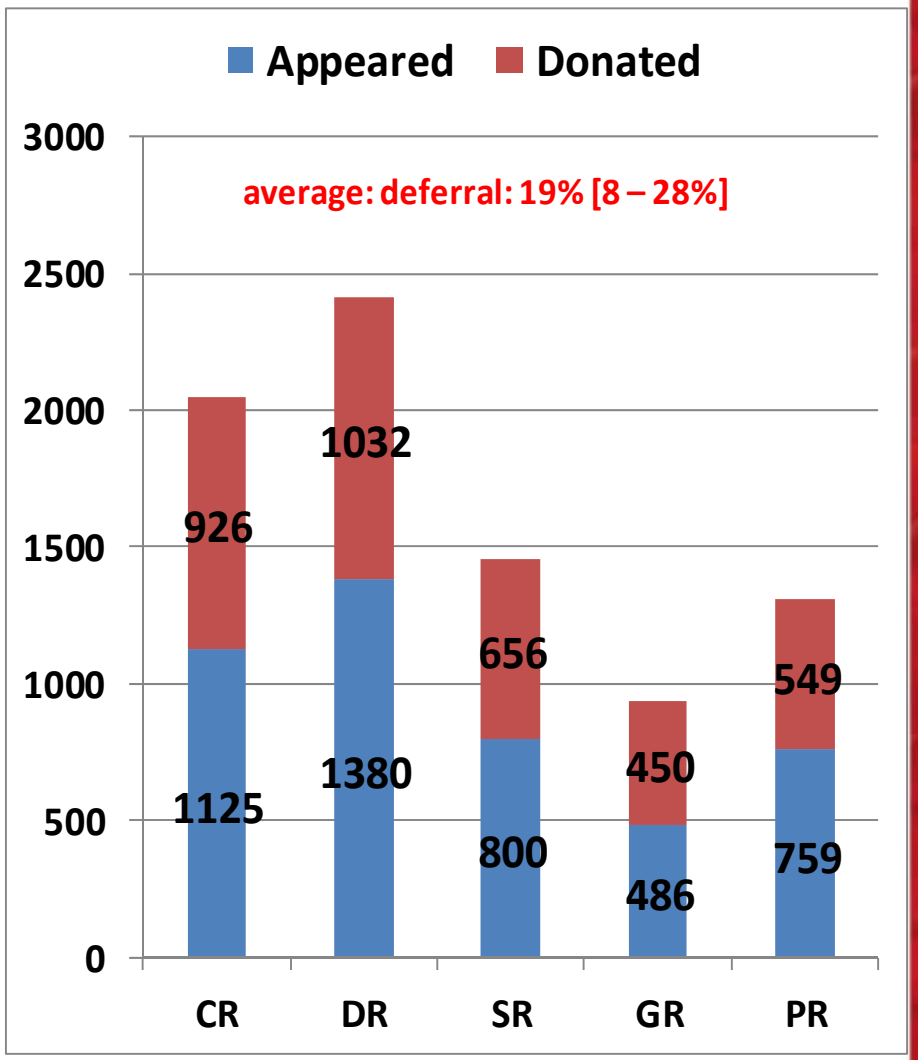
(total donor number is confidential)



Deferrals of plasma donors

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

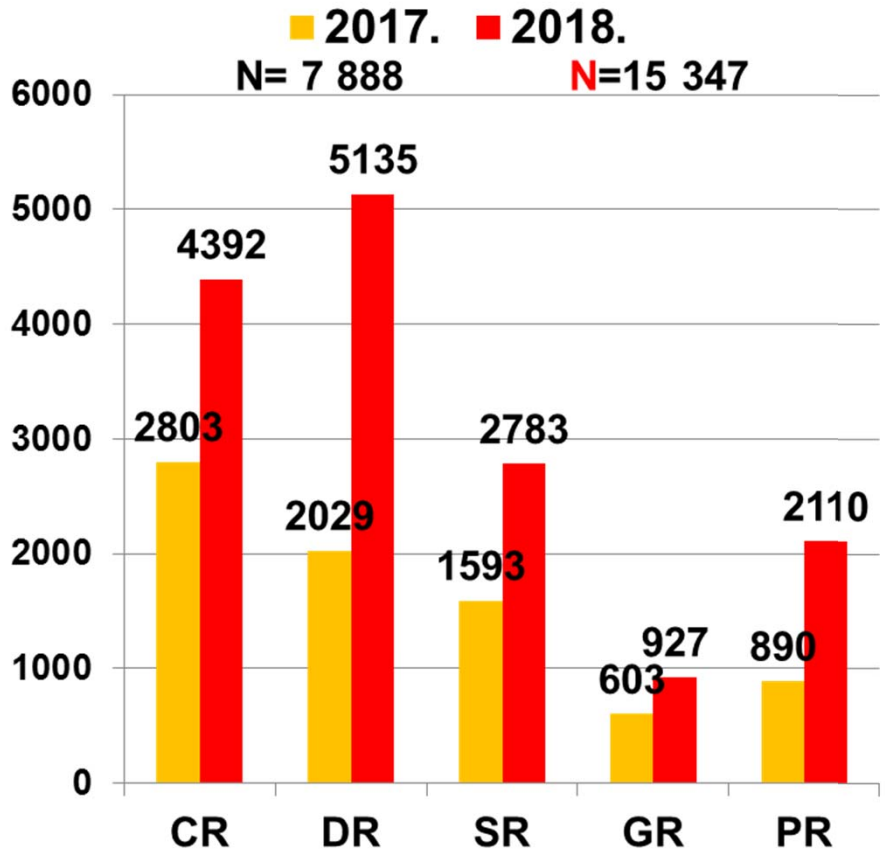
In the database of the HNBTS (eProgesa) 13 (2017.) and 20 (2018.) plasma donors have been deffered in both, too.



Monitorize of the plasmapheresis donors of Whole blood donation's attitude

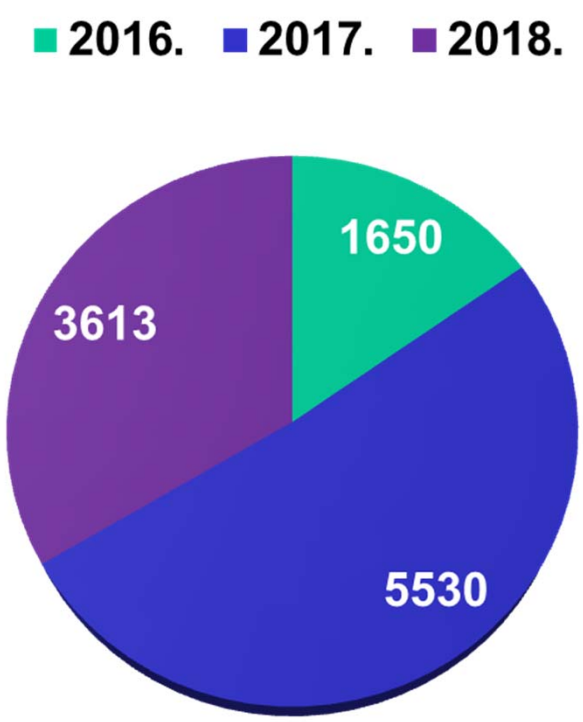
Issued Certificate about the Whole blood donation

(the plasmadonors have visited the HNBTS to give blood)

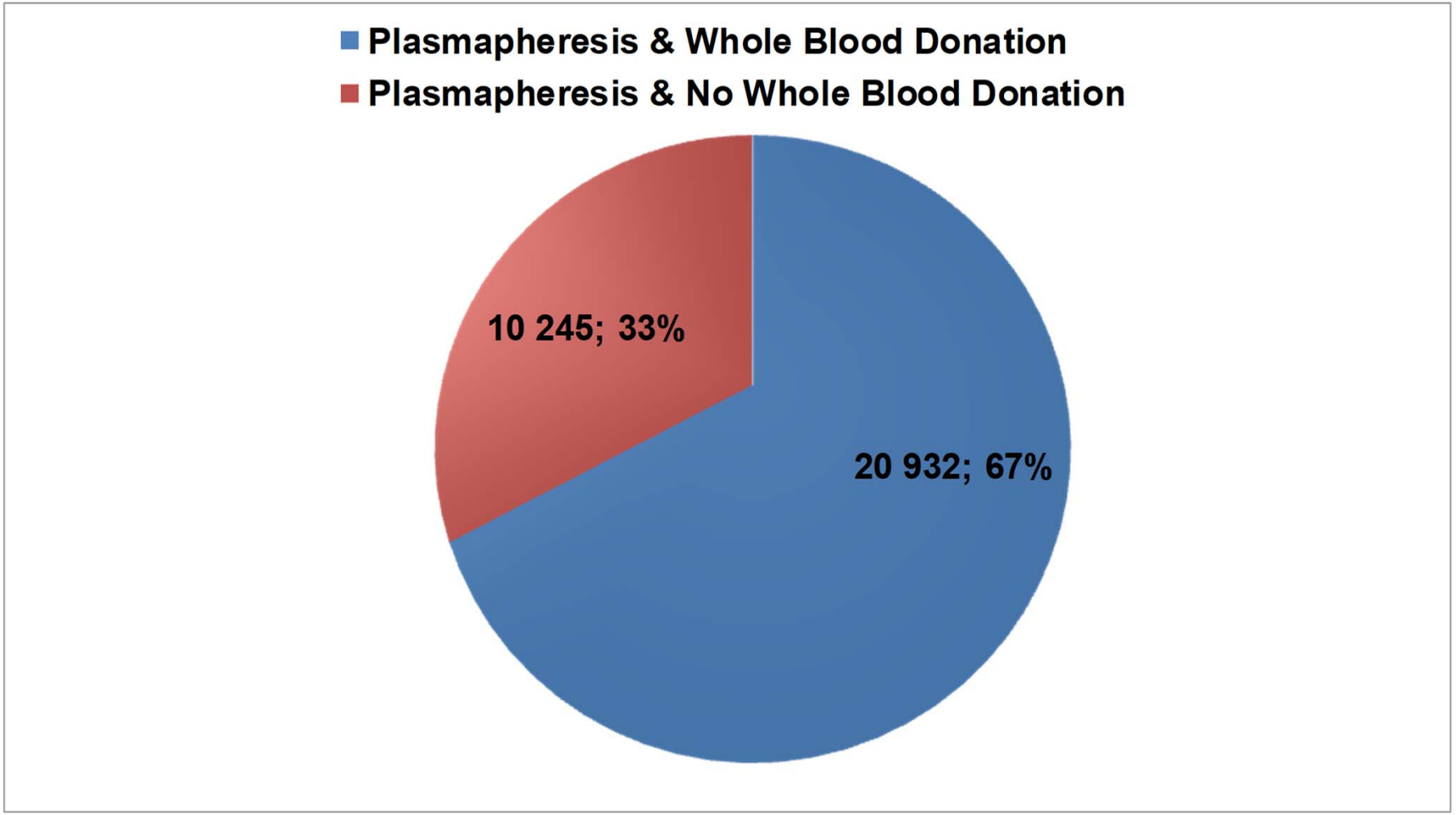


Whole blood donation in the plasmapheresis centres

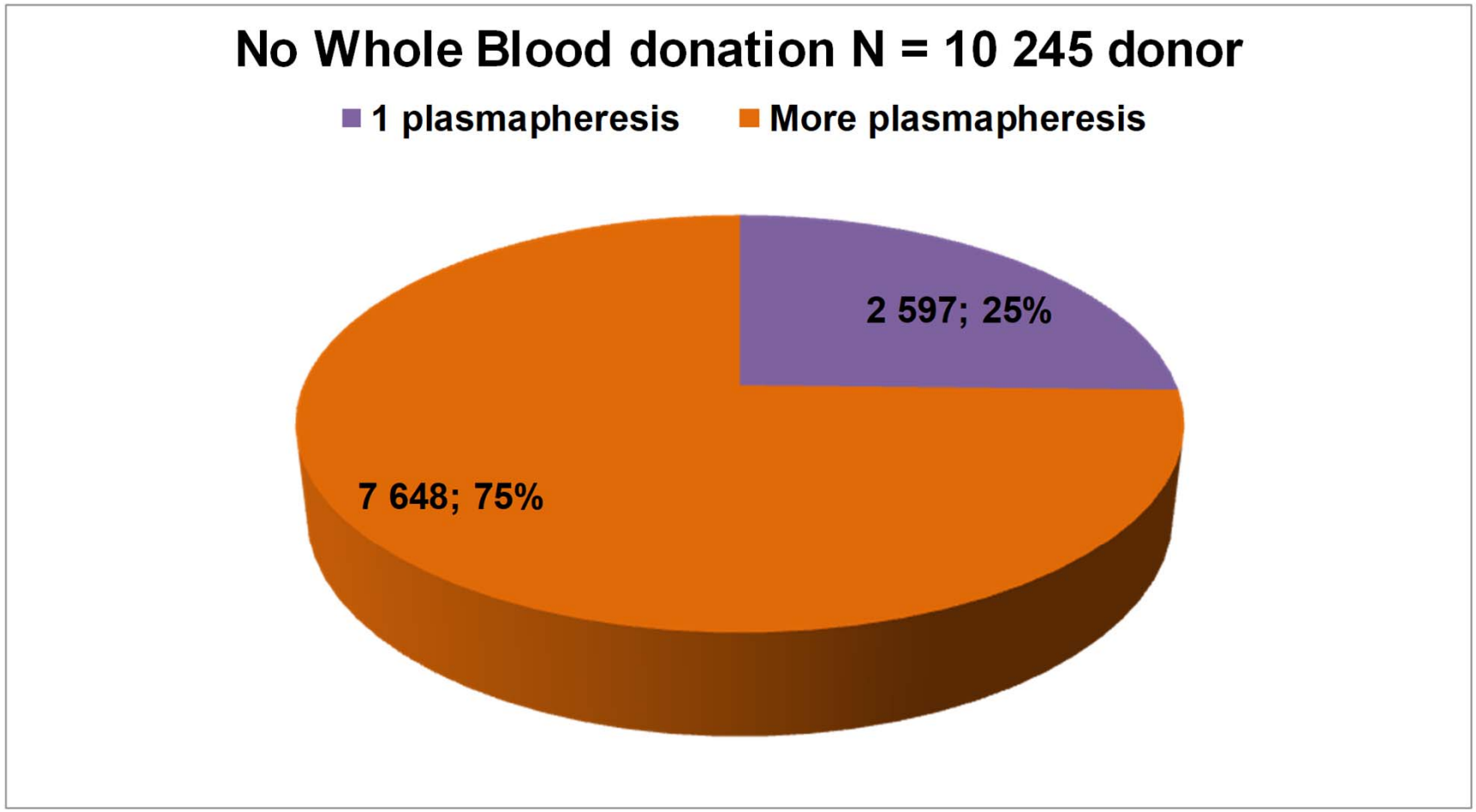
(mobile site, team is belong to the HNBTS)



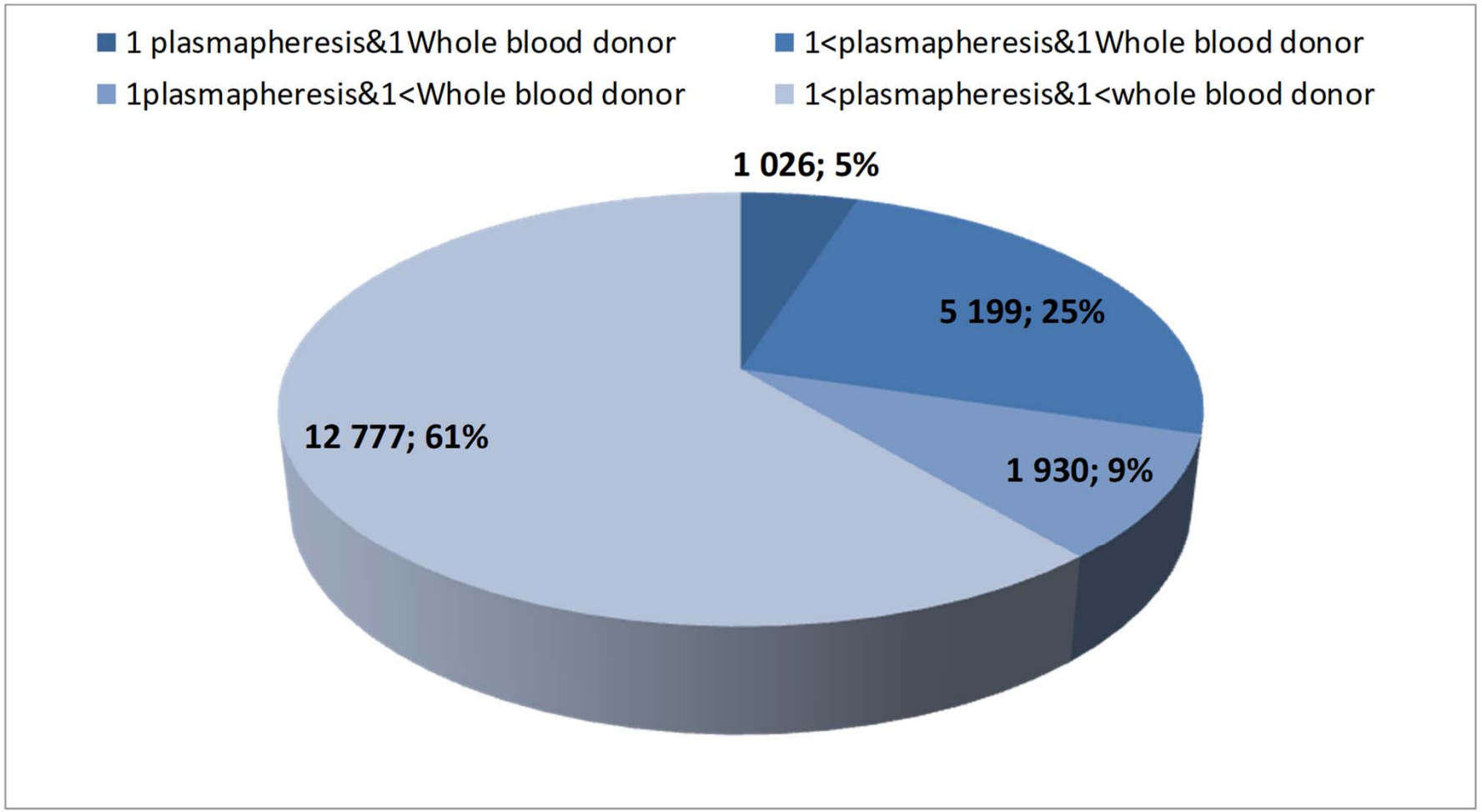
31 177 Donors complaiance of different type of donation 2017.



No Whole Blood donation and different plasma donation attitude in 2017.



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

PATIENT BLOOD MANAGEMENT ITALY

PLASMA ITALIA

CENTRO NAZIONALE SANGUE

Istituto Superiore di Sanità

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.

CENTRO NAZIONALE SANGUE

Agenda

- Founding principles and main figures
- Italy's self-sufficiency
- The Plasma and Plasma-Derived Medicinal Products National Plan 2016 - 2020

CENTRO NAZIONALE SANGUE

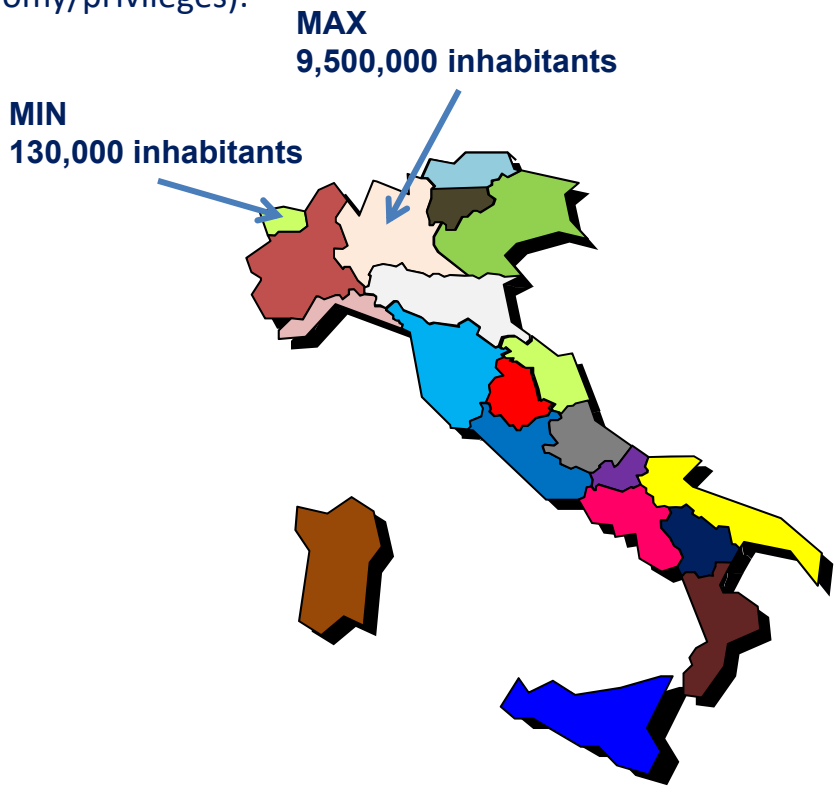
Healthcare governance in Italy

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:

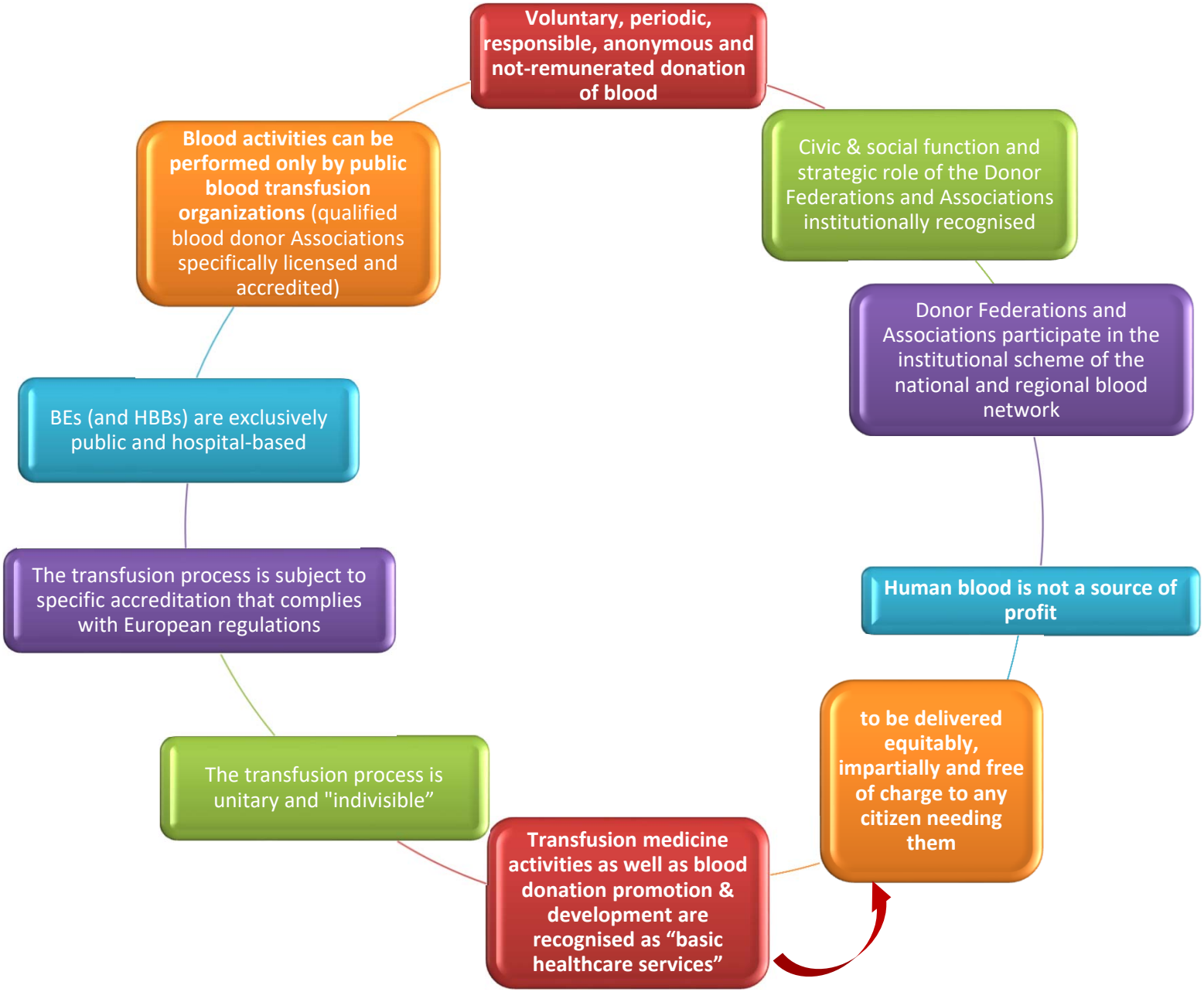
- general healthcare legislation
- transposing EU provisions
- defining "basic healthcare levels" (BHCL)
- controlling BHCL application in the regions
- controlling regional budget balance
- general public health regulation

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)

CENTRO NAZIONALE SANGUE

Italy's Blood System: founding principles



CENTRO NAZIONALE SANGUE

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.

CENTRO NAZIONALE SANGUE

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

CENTRO NAZIONALE SANGUE

Agenda

- Founding principles and main figures
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CENTRO NAZIONALE SANGUE

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.

CENTRO NAZIONALE SANGUE

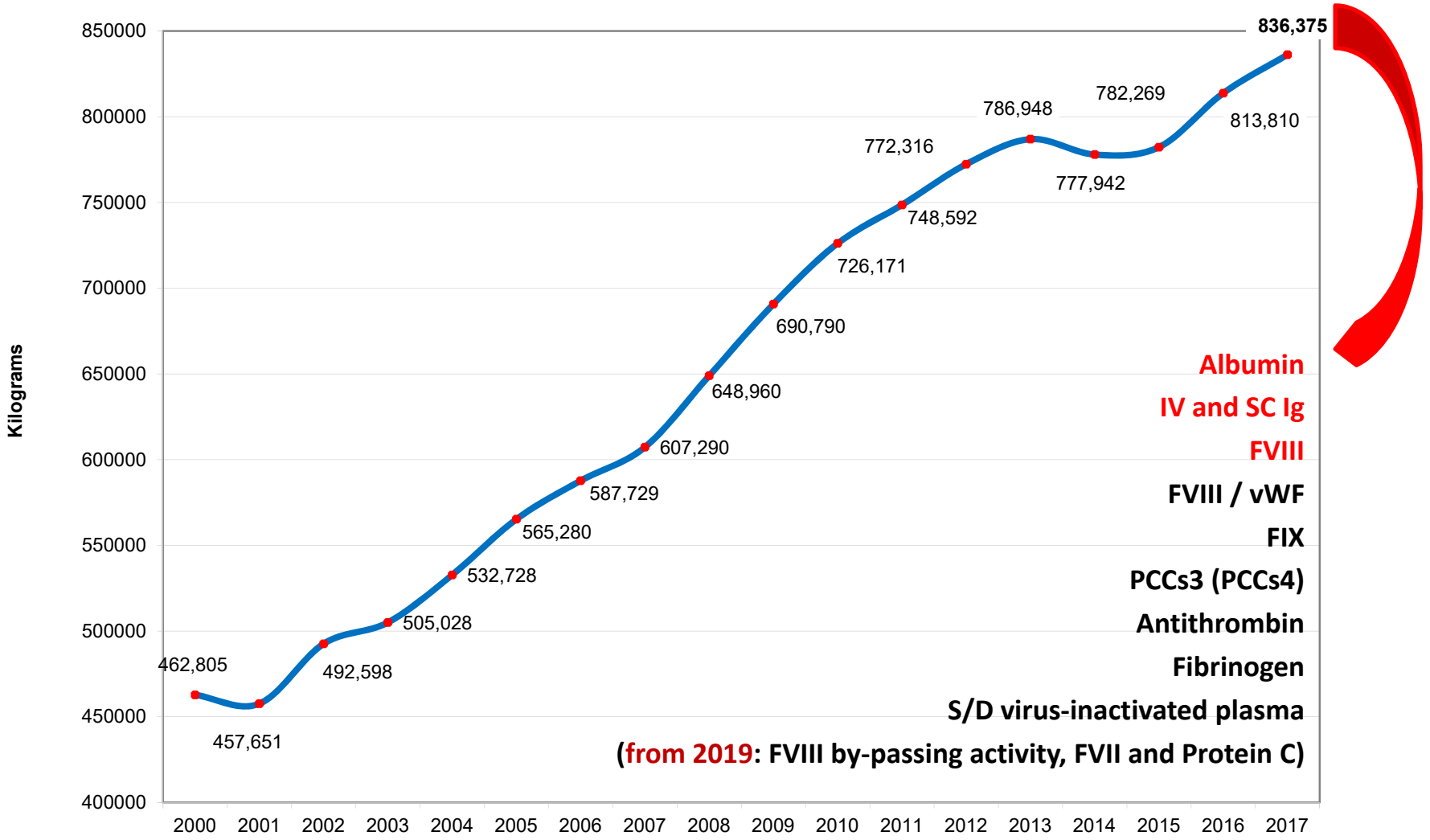
National self-sufficiency of PDMPs

- **"[…] 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."**

Source: Official Journal of Italian Republic no. 9, January 12th 2017. Ministerial Decree December, 2nd 2016 «The Plasma and Plasma-Derived Medicinal Products National Plan 2016 – 2020»

CENTRO NAZIONALE SANGUE

Plasma for fractionation (PfF) 2000-2017

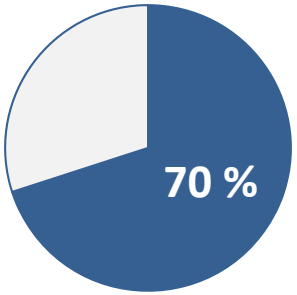


Source: Adapted by the Italian National Blood Centre on data from Fractionation industries, January 2019

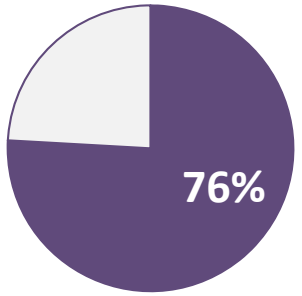
CENTRO NAZIONALE SANGUE

Italy's self-sufficiency in 2017

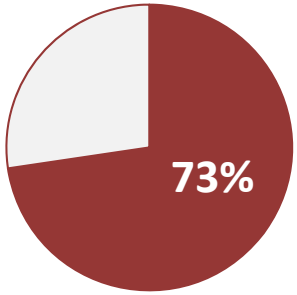
ALBUMIN



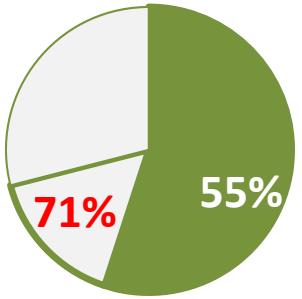
ANTITHROMBIN

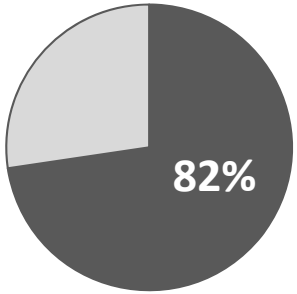


IV IMMUNOGLOBULIN

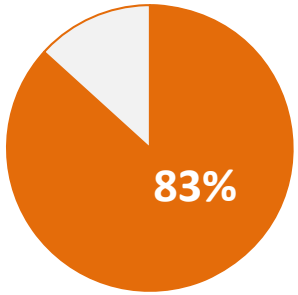


FACTOR VIII



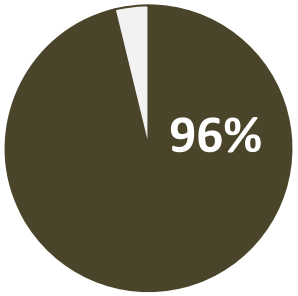


S/D-TREATED PLASMA



FACTOR IX

PCCs3



Candura F, et al. Analysis of the demand of the plasma-derived medicinal products in Italy 2017. Rome: National Health Institute; 2019 (in press)

CENTRO NAZIONALE SANGUE

Agenda

- Founding principles and main figures
- Italy's self-sufficiency
- The Plasma and Plasma-Derived Medicinal Products National Plan 2016 - 2020

CENTRO NAZIONALE SANGUE

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.

CENTRO NAZIONALE SANGUE

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

CENTRO NAZIONALE SANGUE

Plasma and PDMP National Plan

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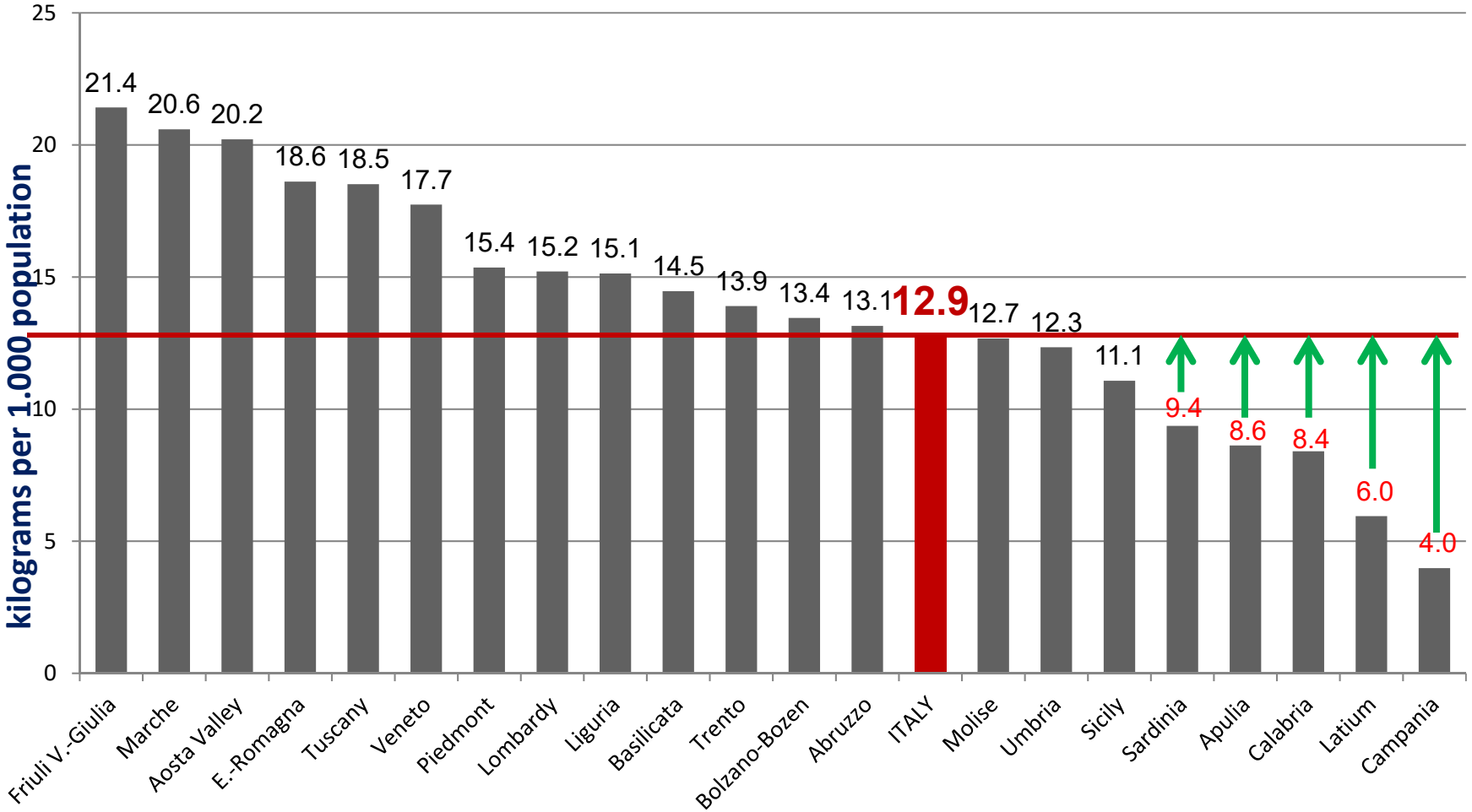
CENTRO NAZIONALE SANGUE

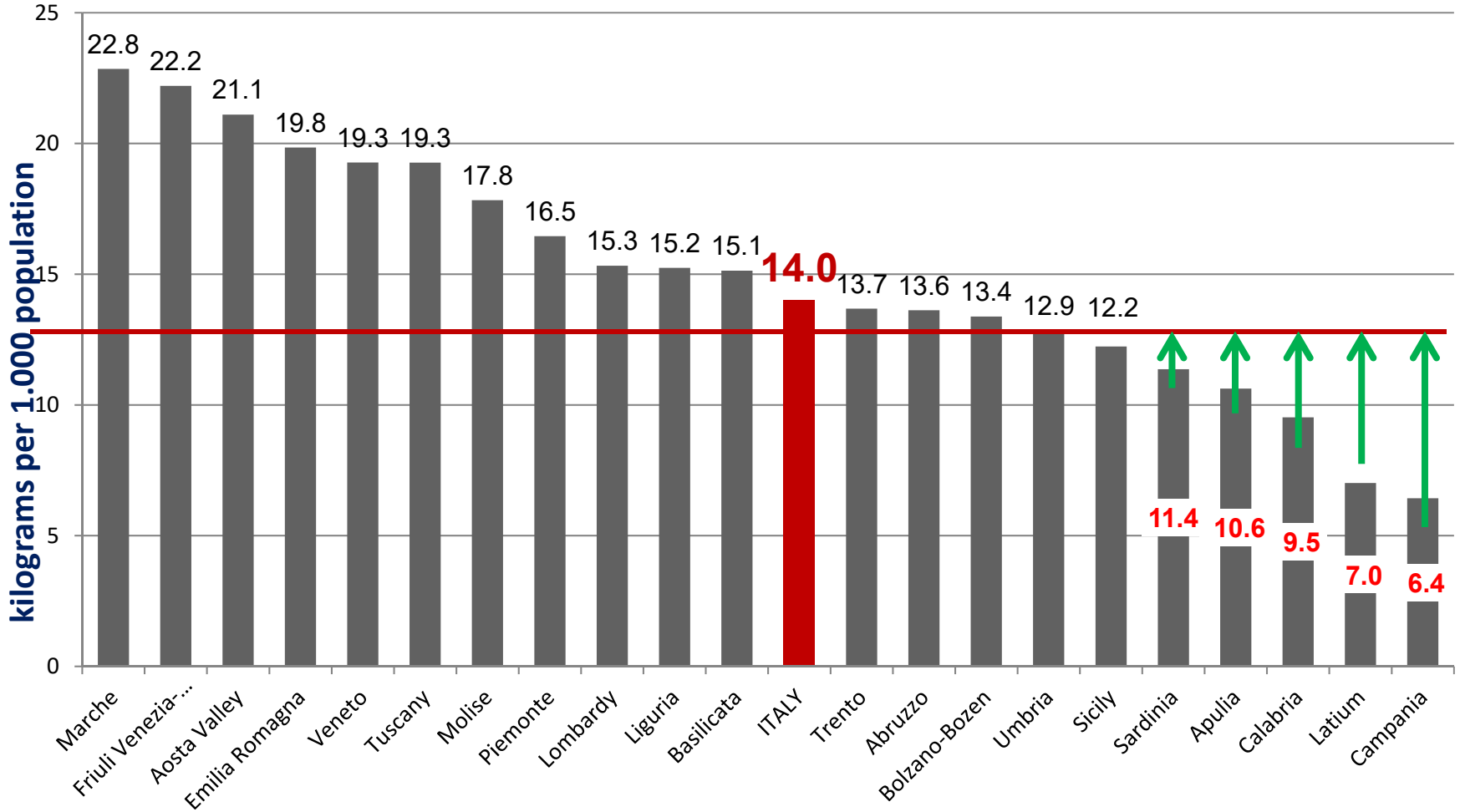
PfF 2015



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

CENTRO NAZIONALE SANGUE

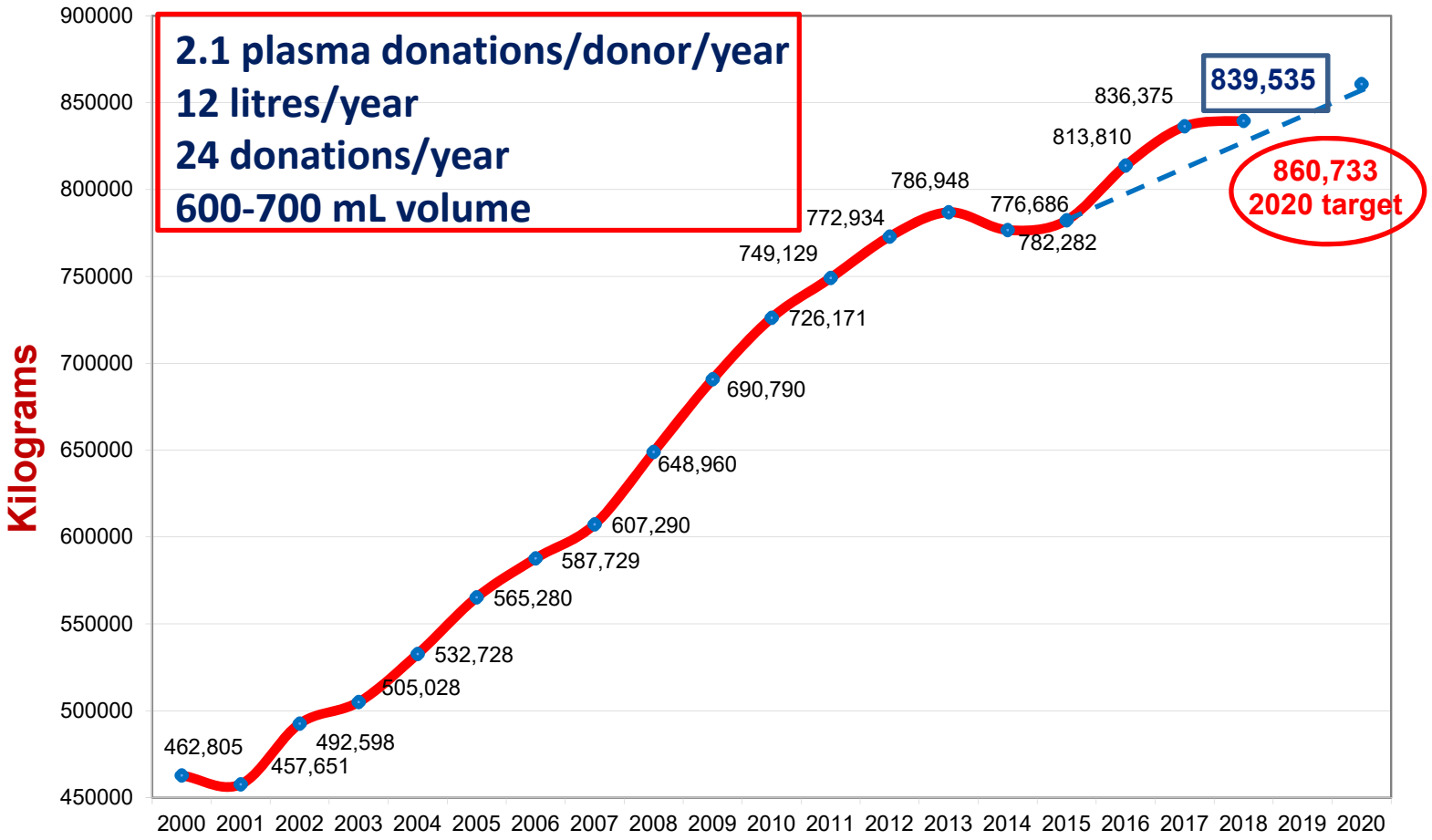
PfF 2018



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

CENTRO NAZIONALE SANGUE

PfF 2000-2018 and PNP 2020 target



- Official Journal of the Italian Republic no. 9 January 12th 2017. Ministerial Decree 2 December 2015
- Adapted by the Italian National Blood Centre on data from Fractionation Industries. January 2019

CENTRO NAZIONALE SANGUE

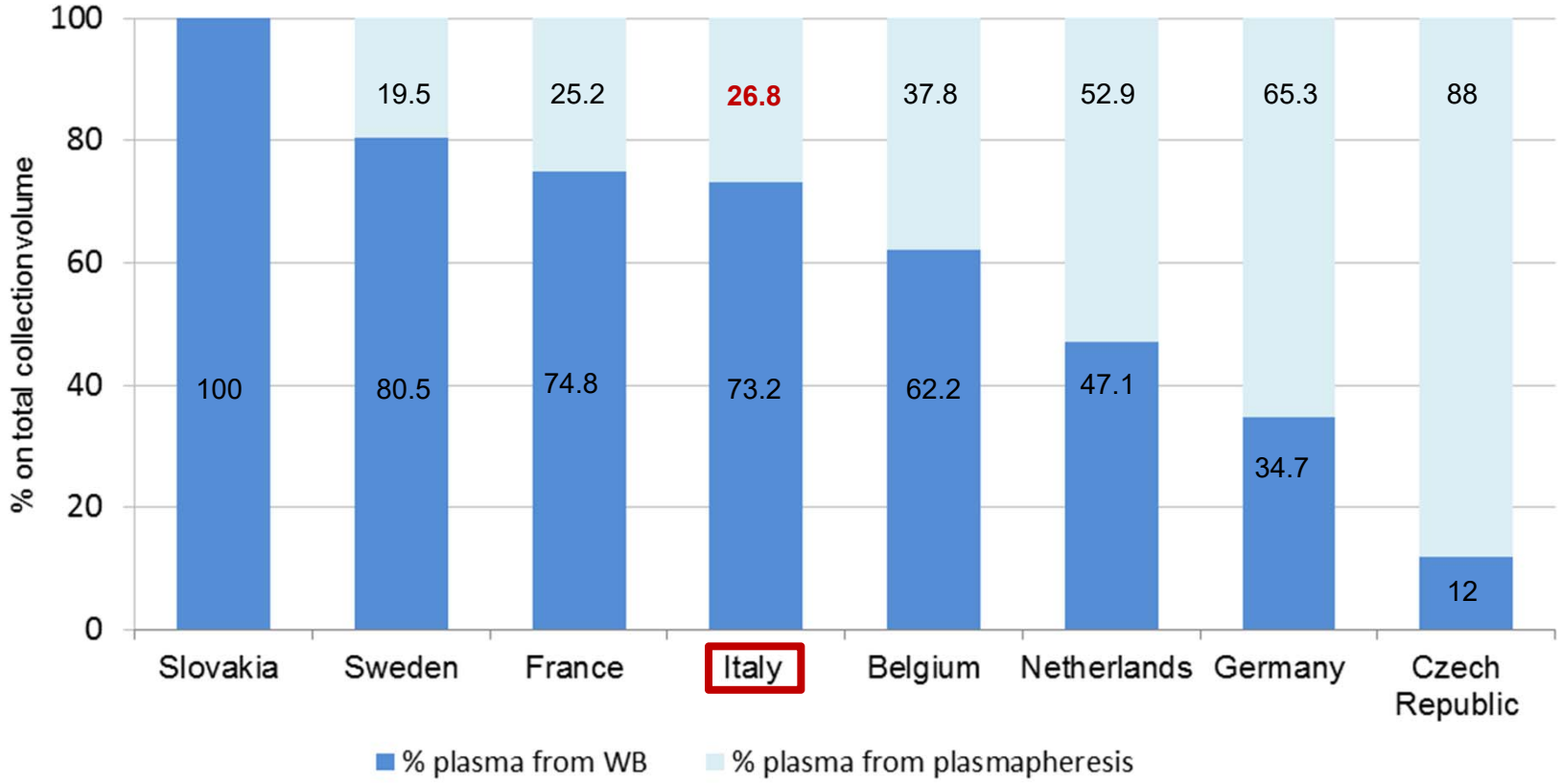
Plasma and PDMP National Plan

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.

CENTRO NAZIONALE SANGUE

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

  } **2020 targets**
- 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)

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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]

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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!)

CENTRO NAZIONALE SANGUE

ONLY ONE

PLASMA ITALIA

CENTRO NAZIONALE SANGUE

Istituto Superiore di Sanità

Thanks for your attention!

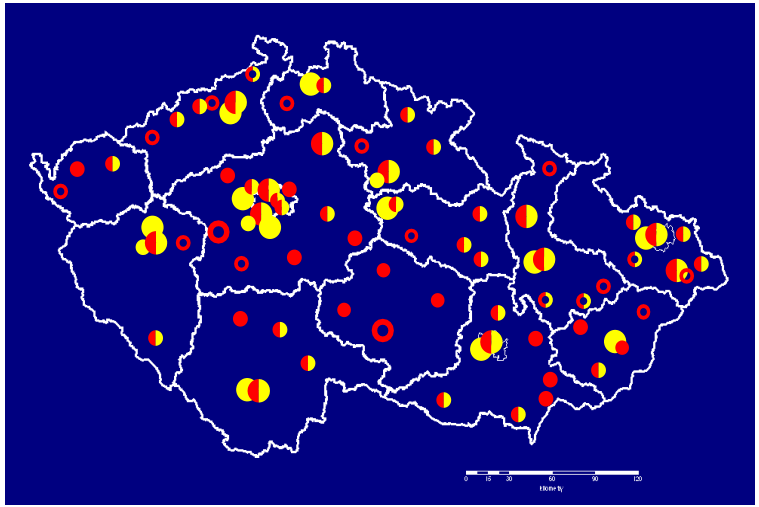
PLASMA COLLECTION in the CZECH REPUBLIC

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 nonremmunerated donation:

(nearly all donations in hospital-based BTS)

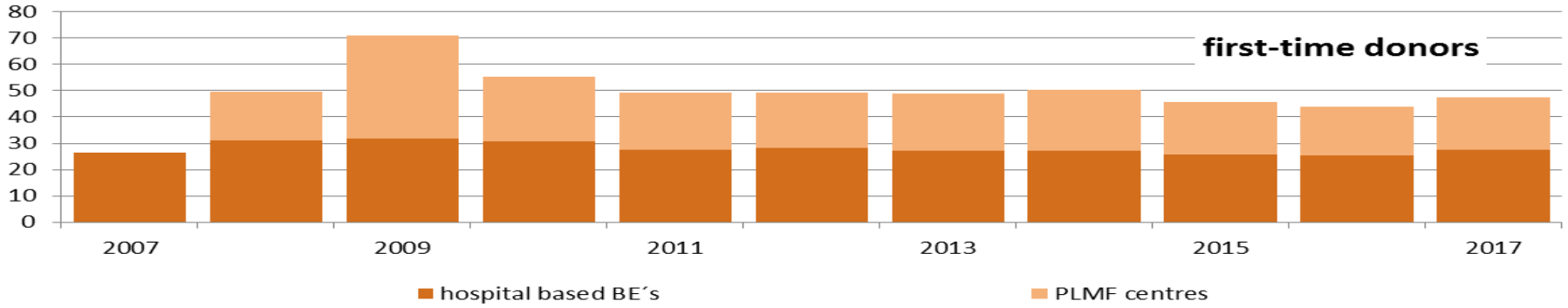
- reimbursement of travel expenses and direct costs
- small refreshment
- possible tax deduction

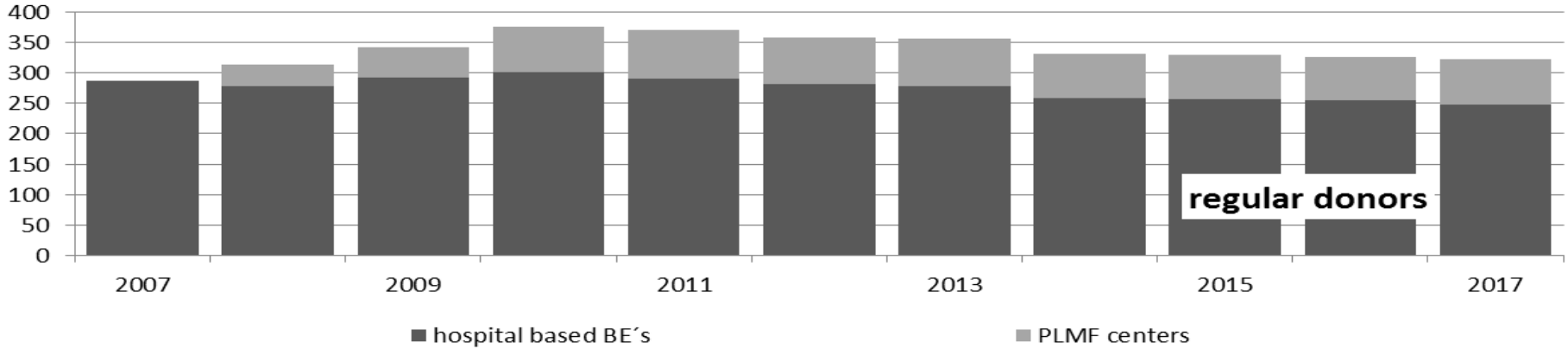
Compensated donation:

(vast majority of plasma collections in plasma-centres)

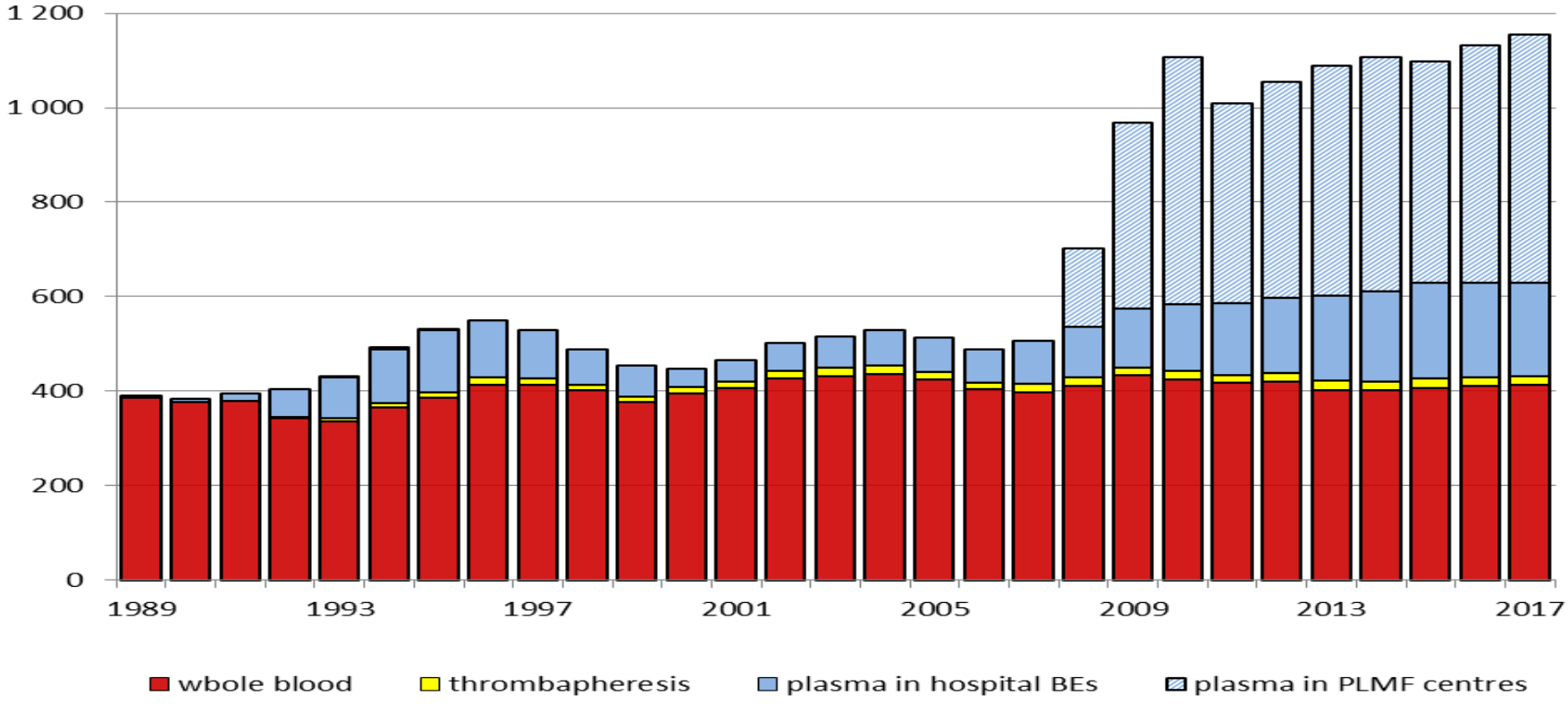
- compensation of time lost, inconvenience, travel expenses ...
  (max. amount regulated by law = cca 25 Euros / donation)
- small refreshment

Blood donors regular / first time (in thds.)





Blood / plasma donations (in thds.)



Age of donors in hospital-based BTS

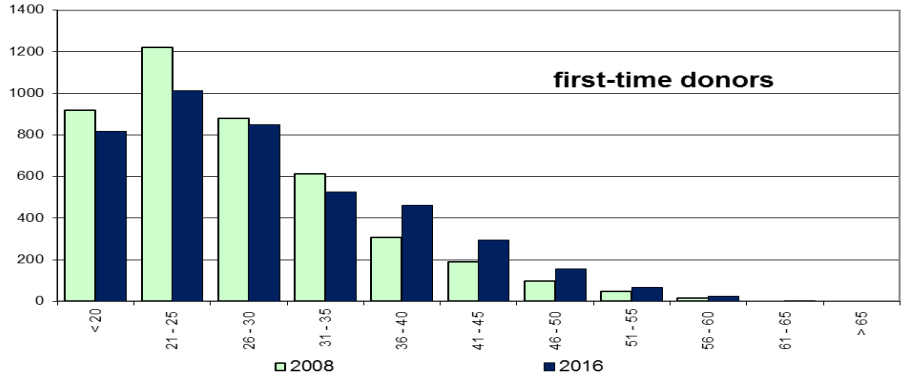
comparison 2008 / 2016

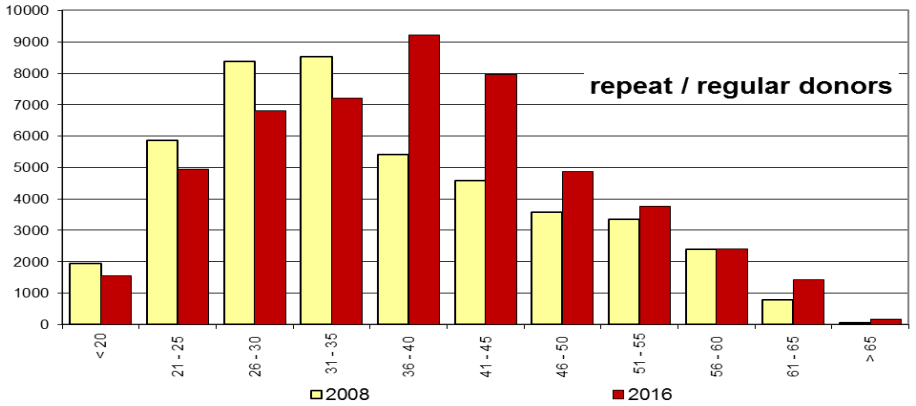
No. and percentage of young first time-donor decreased

mean age of repeat / regular donors increased

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

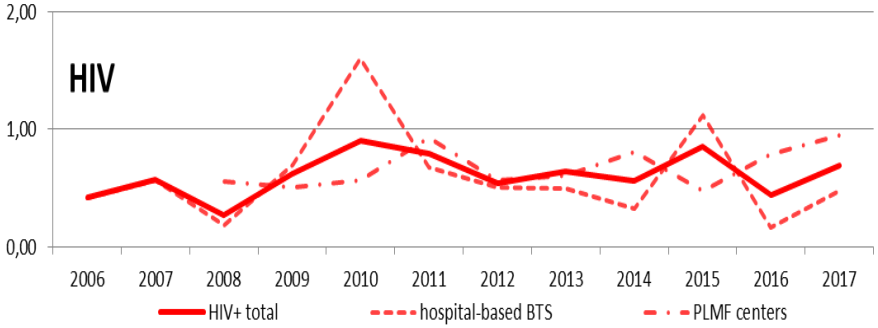
NB: data from plasma centers in CZ are not available

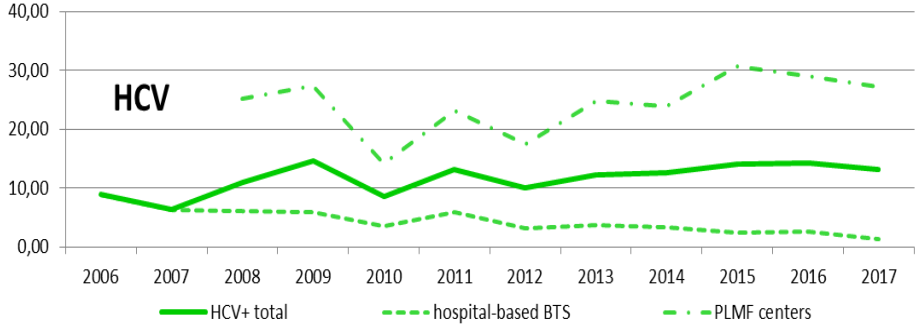


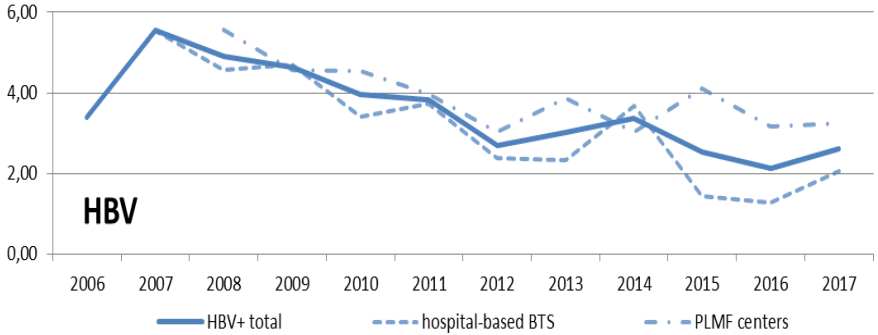


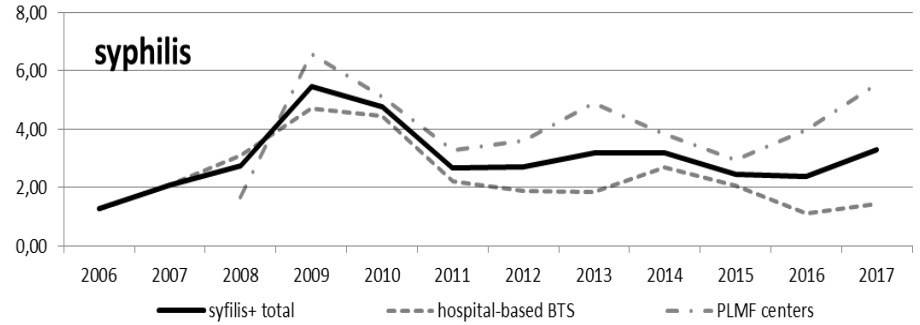
Infection rate in blood donors

(hospital based BTS versus plasma-centers)



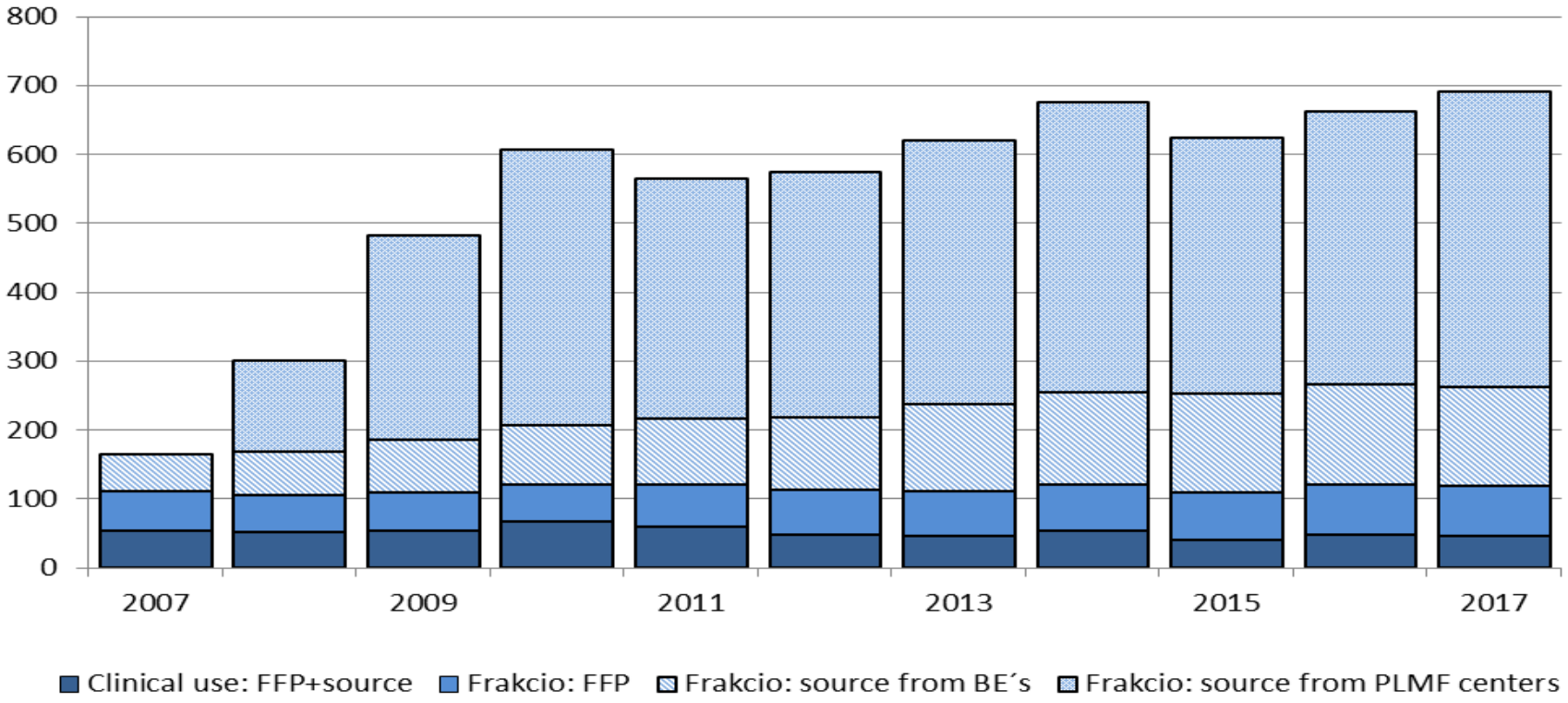






number of positive donations / 100 000 donations

Plasma production / usage (litres in thds.)



Distribution of CZ plasma for fractionation

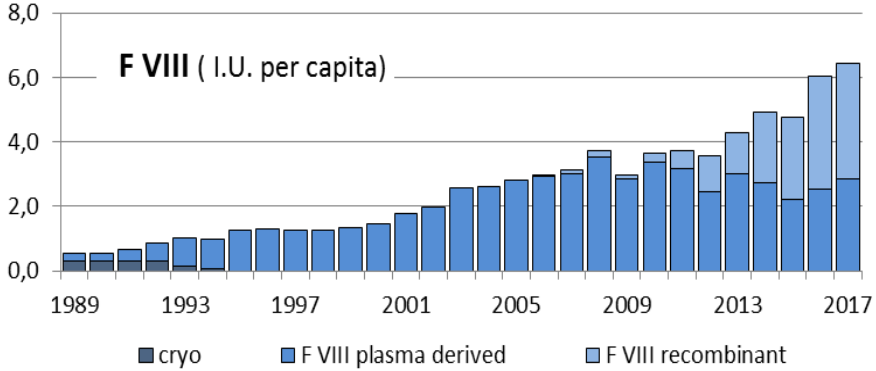
in 2017:

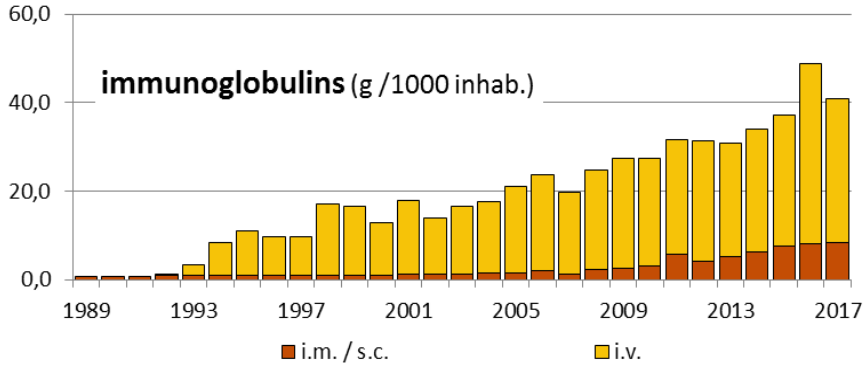
• WB derived plasma	72,3 thds. litres
• source plasma from BE´s	143,4 thds. litres
• source from plasma-centers	429,0 thds. litres
Total	644,7 thds. litres

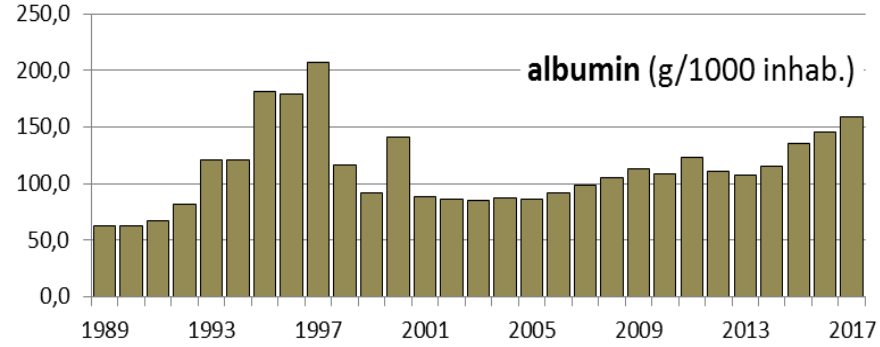
eg.

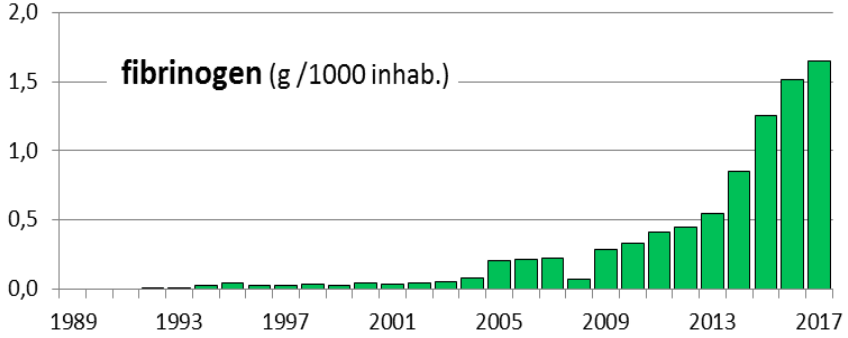
• WB derived plasma	6,9 l / 1000 inhab.
• source plasma from BE´s	13,4 l / 1000 inhab.
• source from plasma-centers	40,8 l / 1000 inhab.
Total	61,1 l / 1000 inhab

Distribution of plasma products in CZ









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 compeet 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 Goverment 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 limmits 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 exapmle 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 intravenus 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 revison 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 prelimenary 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

Zavod Republike Slovenije
za transfuzijsko medicino
Blood Transfusion Centre of Slovenia

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 pacients 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

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za transfuzijsko medicino
Blood Transfusion Centre of Slovenia

- 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

Belgian
Red Cross
Flanders
helps
people help

Facts & Figures Belgium Blood Banking system

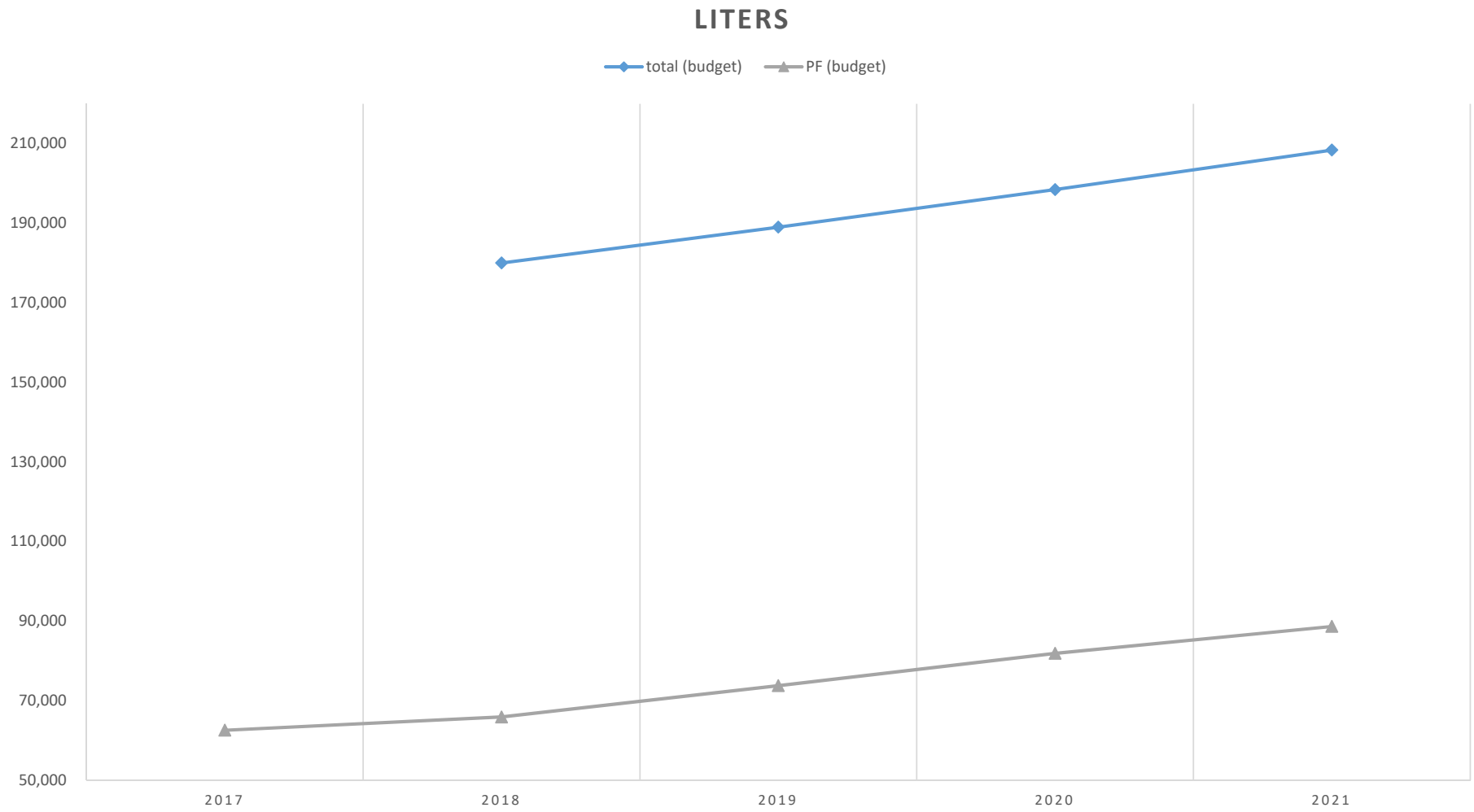
- 11,5 million inhabitants
- Separate legislation
  - Labile blood products
  - Stable blood products
- Universal VNRD (whole blood, plasma, platelets)
- Responsibilities
  - Federal Ministry of Health
  - Competent authority: Federal Agency for health products

4 Licensed Blood Establishments

	Blood institution	% RBC
Flanders	Belgian Red Cross-Flanders	62
Frenchspeaking Belgium	Croix Rouge de Belgique-Comm Francophone	32
	CHU Charleroi	5
	CHU Mont-Godinne	1

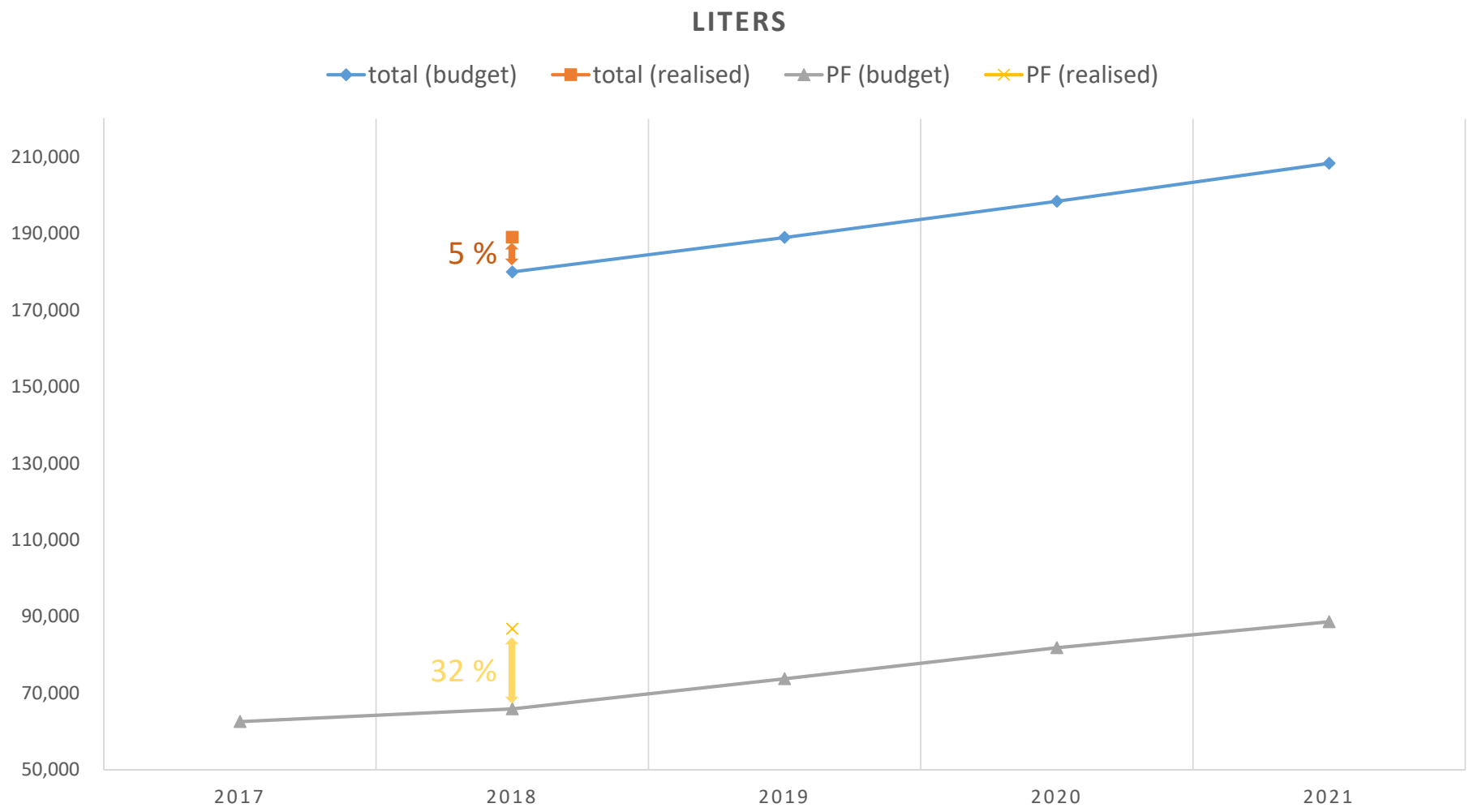
Belgian Red Cross Flanders
helps people help

Initiative Belgian Government: budget



Belgian
Red Cross
Flanders
helps
people help

Initiative Belgian Government: realisation



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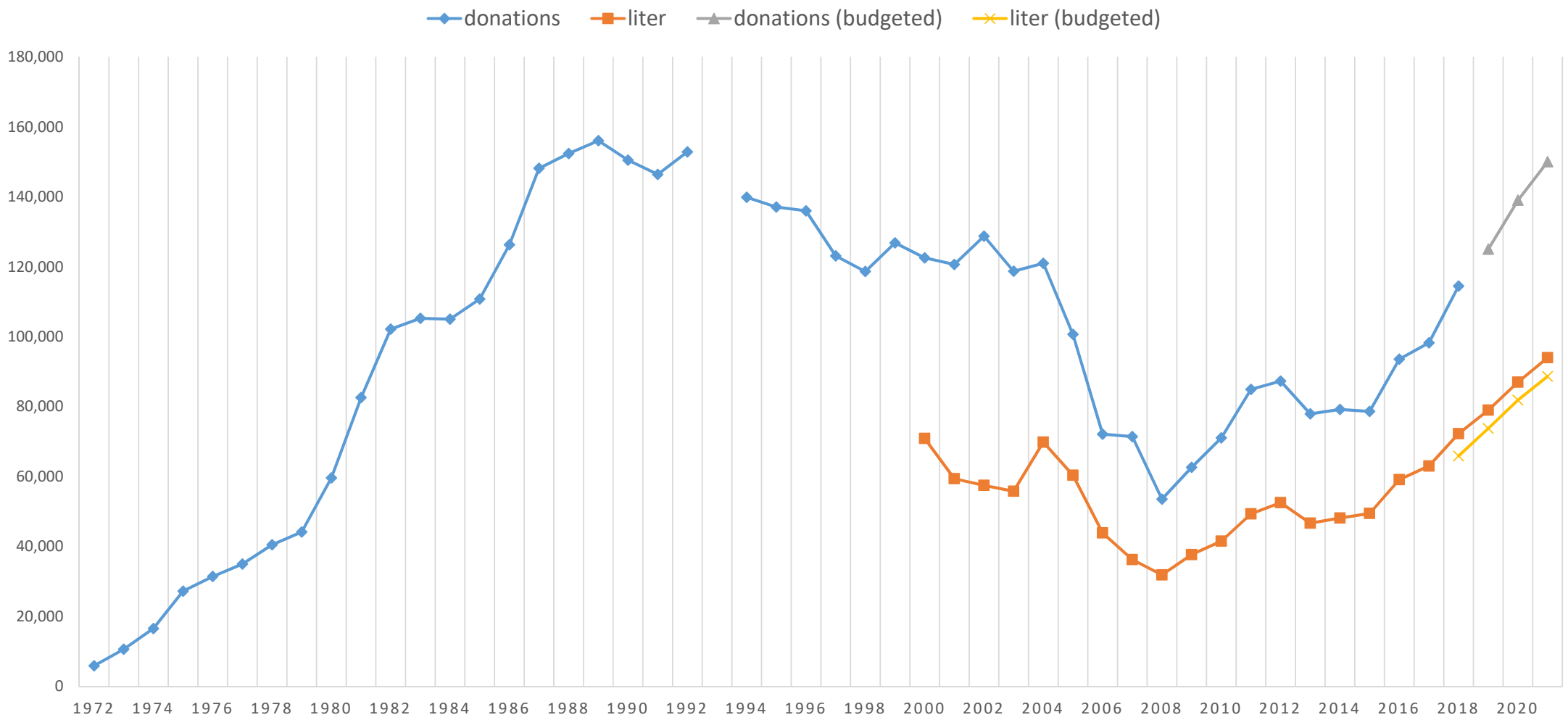
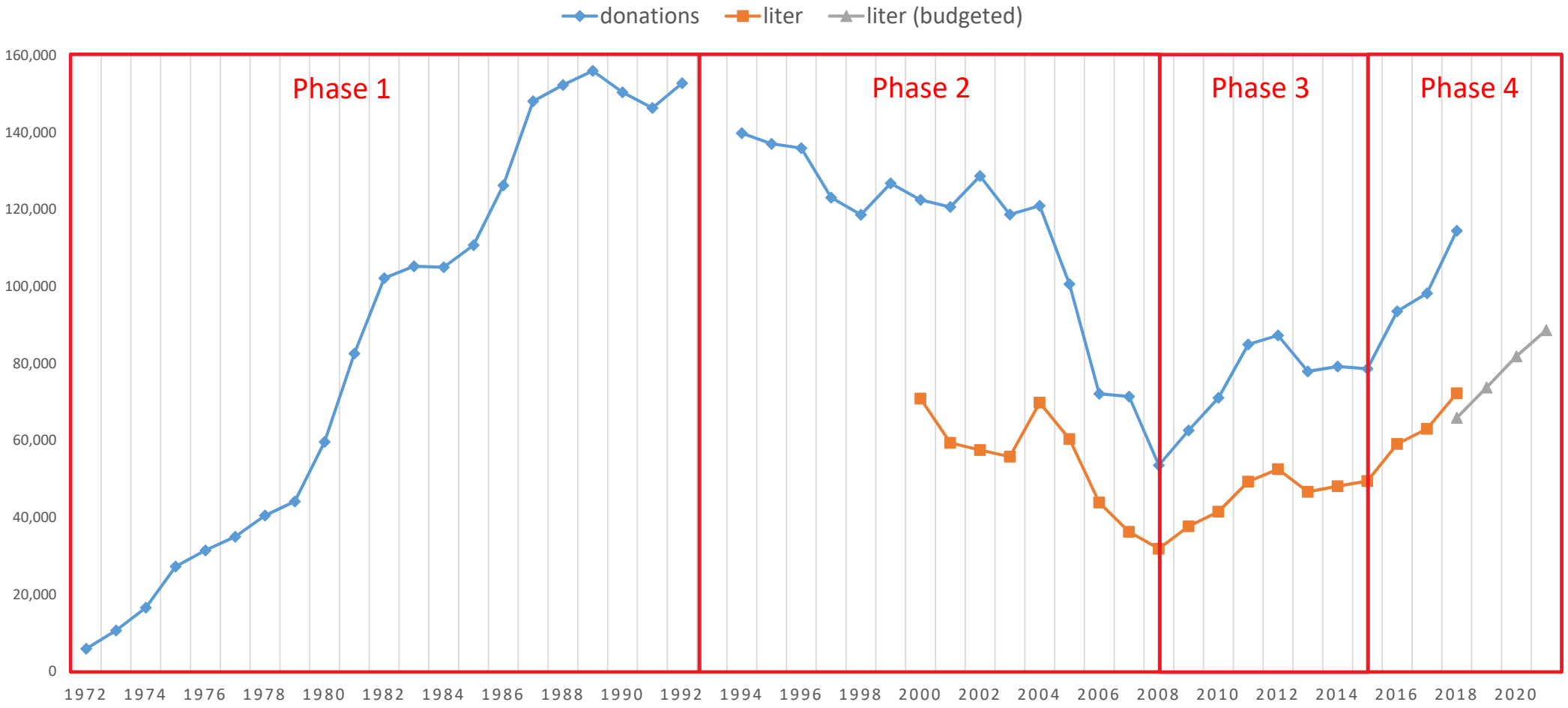
Historical Overview Plasmapheresis *(Flanders, Belgium)*



Historical Overview Plasmapheresis *(Flanders, Belgium)*

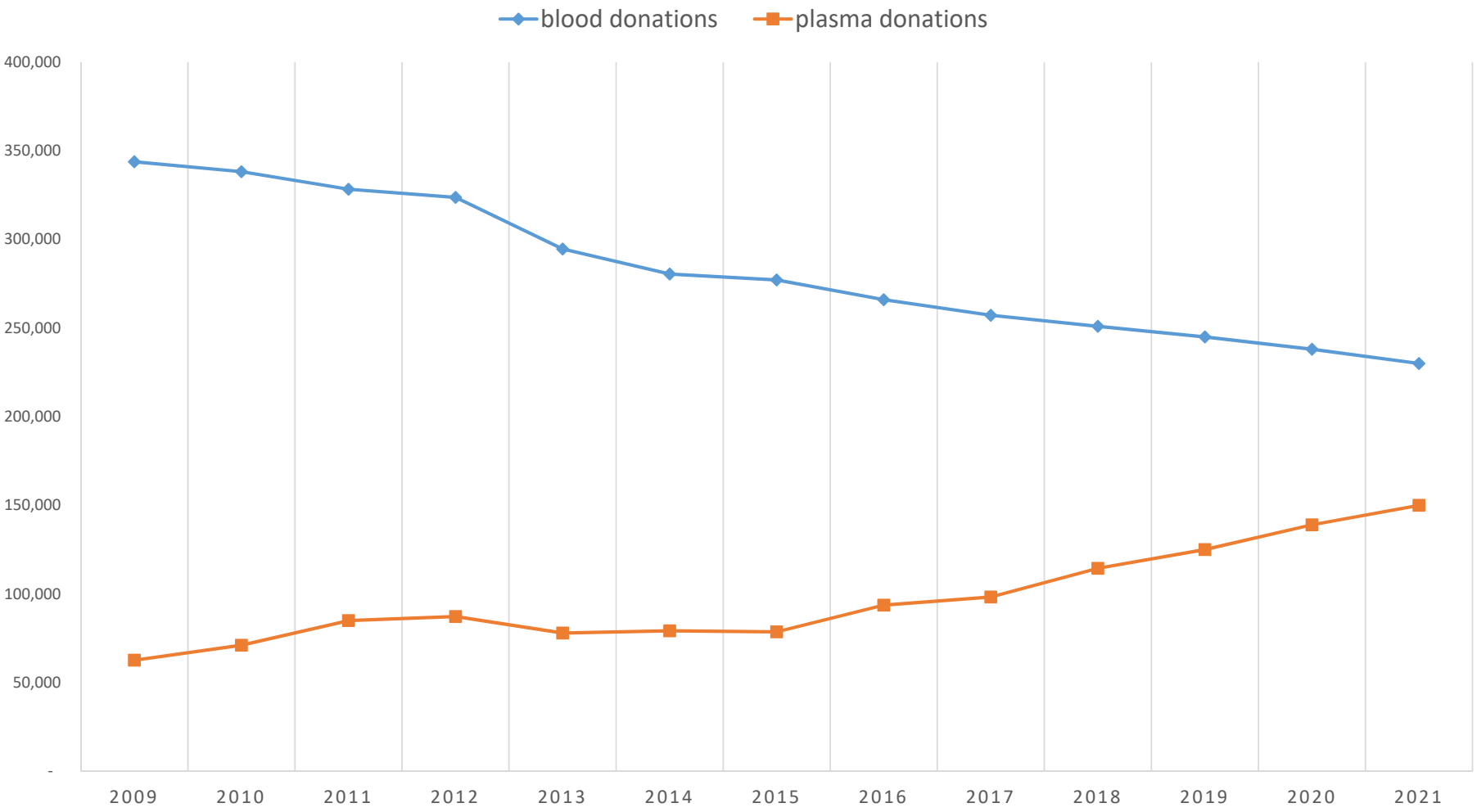


Analysis

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)*



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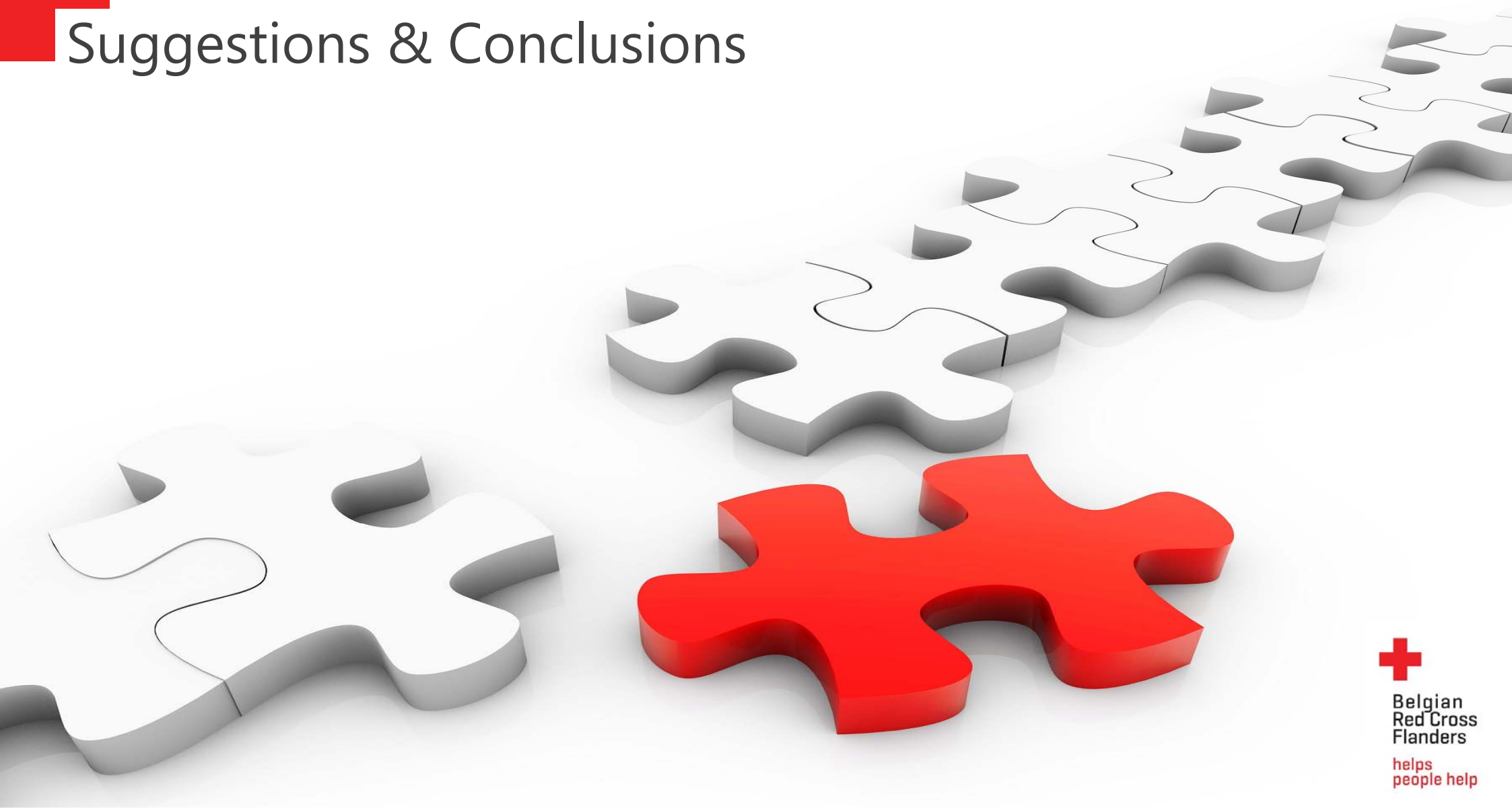
Suggestions & Conclusions



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