



**CENTRO
NAZIONALE
SANGUE**



Contract manufacturing from the public plasma provider's perspective

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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

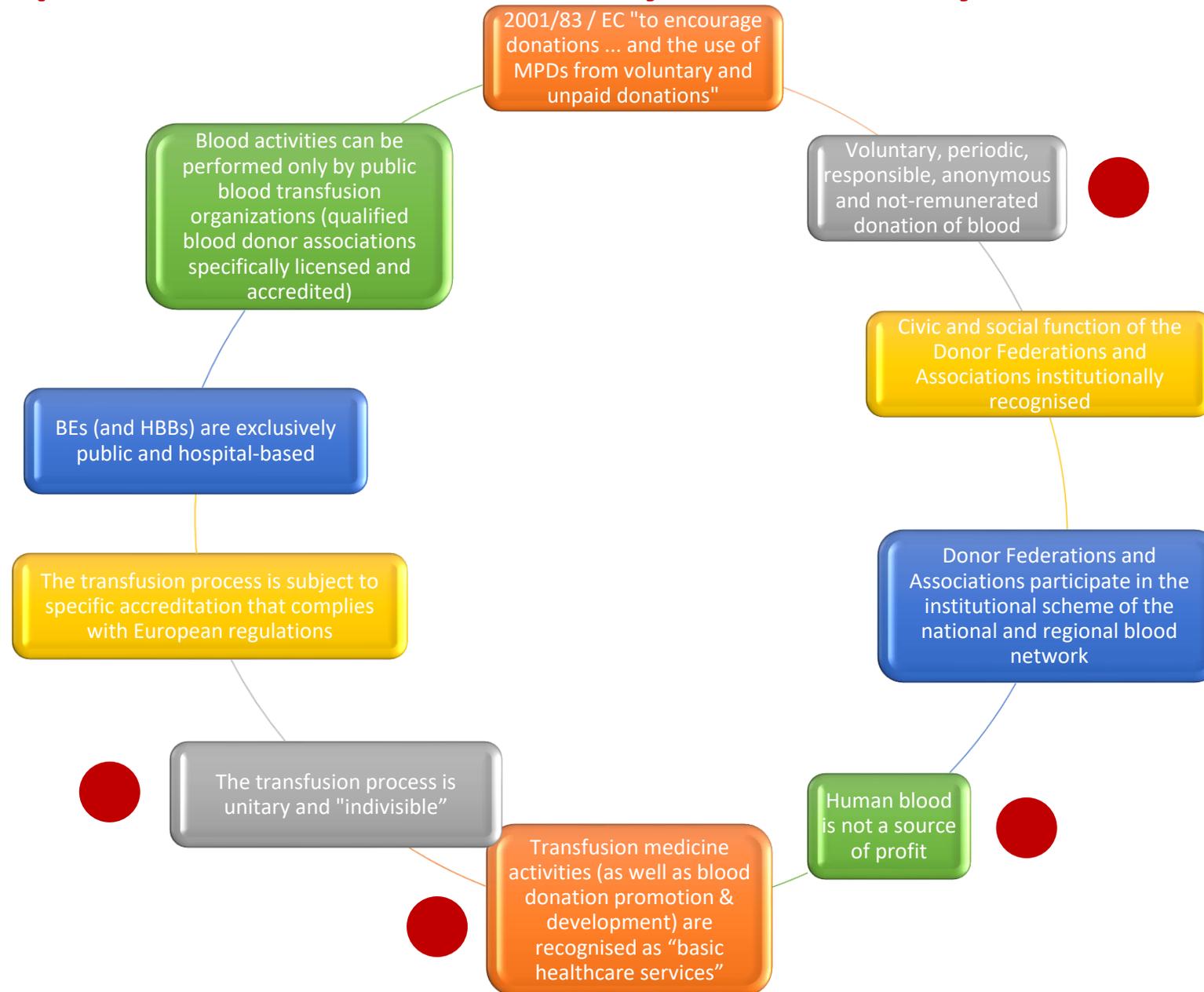
NO AI used in this presentation

Agenda

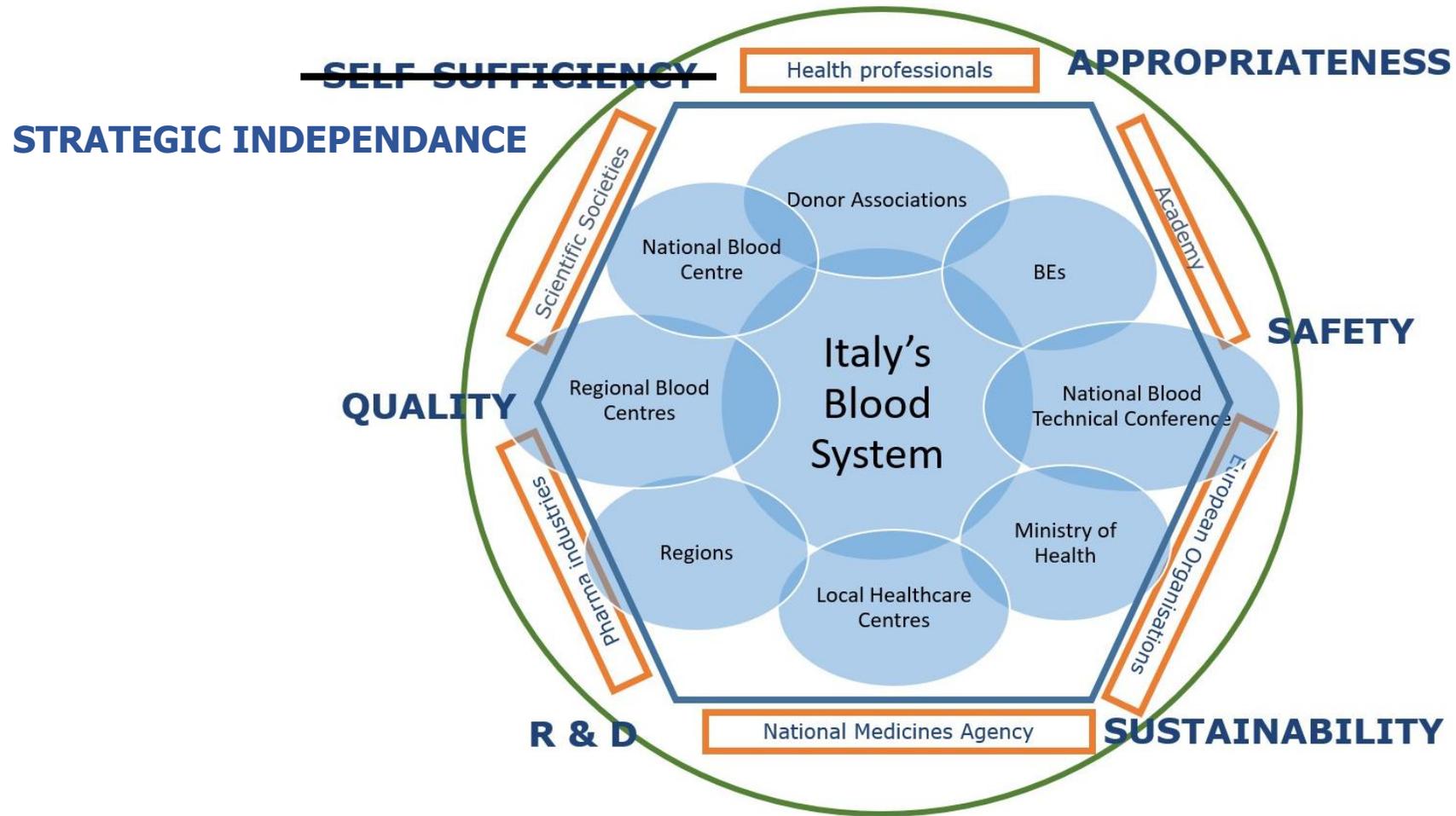
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**THE ITALIAN BLOOD SYSTEM:
founding principles and regulatory context**

Ethical principles and social value of Italy's donation System



Stakeholders and Strategic Objectives



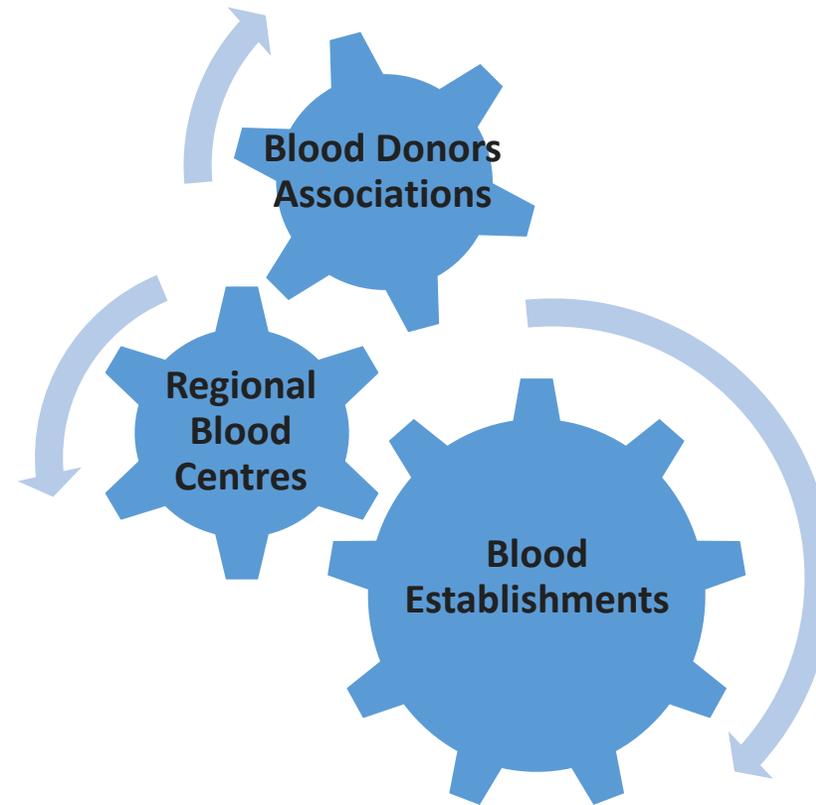


The Italian Blood System - Law October 21, 2005

Regional Blood Centres:

in each of the 21 regions, a Regional Blood Centre is established by law. The regional Blood Centres coordinate the related local networks of Blood Establishments and Blood Collection Units, complying with national regulation and self-sufficiency, quality and safety plans

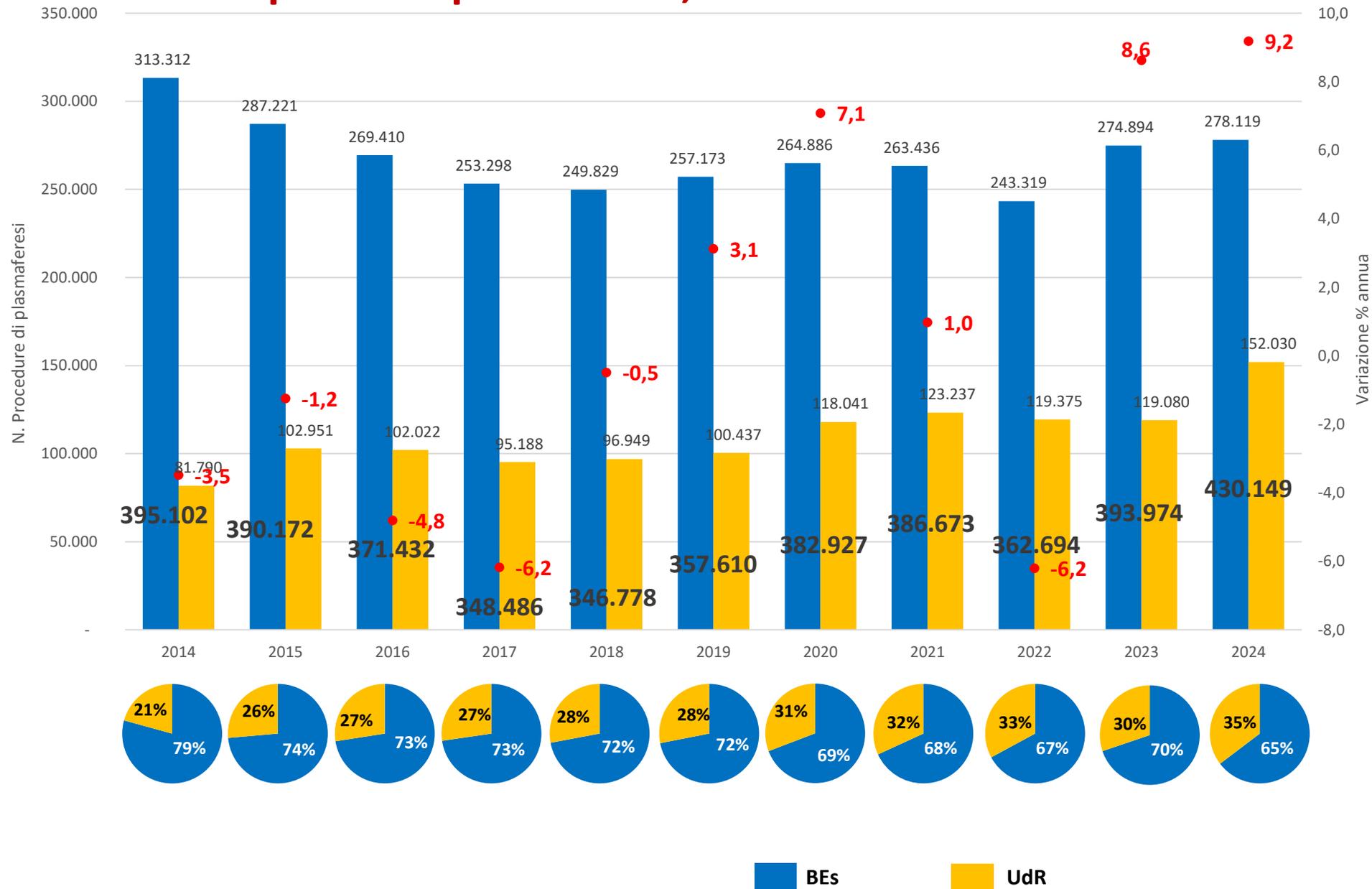
Blood Establishments: in addition to performing blood and blood component collection, processing, testing, storage and distribution, most Blood Establishments also work as hospital blood banks



Blood Donors Associations: there are four main blood donors organisations (AVIS, FIDAS, FRATRES, CRI) that are highly involved in the blood donor management. By law, they can run Blood Collection Units upon the release of specific regional authorization and accreditation, under the technical control of both Blood Establishments and Regional Blood Centers.



Plasmapheresis procedures, 2014 - 2024



Between 2014 and 2024, 35,047 (+9%) increase in plasmapheresis procedures. The increase is mainly represented by procedures performed at UdR (+70,240 or +85.9%), while -35,193 (-11.2%) procedures performed in BEs.

Regulatory context

EU Regulatory Framework

Italian Law



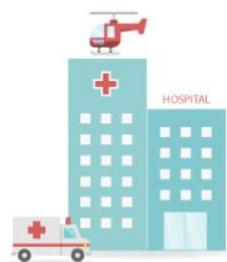
Blood Establishments

They collect plasma coming from the voluntary donations.



Authorized companies

They carry out the plasma industrial processing for the production of plasma derived medicinal products.



Pharmacies operating in hospitals

They administer plasma derived medicinal products to patients.

EU rules on the collection and control of blood components (GPGs)

EU rules for the processing, storage and transport of plasma as a raw material for medicinal products (GMPs)

EU rules that regulate the market and competition

EU code relating to medicinal products for human use

The Italian Blood System and PDMPs

Law no. 219 October 21, 2005

Founding Principles

Art. 1
National Self-sufficiency

Art. 2
VNRB donation
PDMPs production is part of Transfusion medicine activities

Art. 5
Transfusion medicine activities (including the PDMPs production) are BHCLs

Art. 15 (PDMPs production)

4 Ministerial Decrees
April 12, 2012
December 5, 2022
December 19, 2022

Ministerial Decrees
~~December 5, 2014~~
July 22, 2024
November 6, 2024

Art. 16 (import-export)

State-Regions Agreement
February 7, 2013

Ministerial Decrees
December 2, 2016
April 24, 2018

Instruments

State-Regions Agreements
~~October 20, 2015~~
June 17, 2021

State-Regions Agreement
~~March 14, 2016~~
July 8, 2021

Lgs.D 261/2007

Art. 26

Ministerial Decree
December 2, 2016

Plasma and PDMPs National Plan 2017 - 2021

The Italian Blood System and PDMPs - Relevant points

Art. 15 (PDMPs production)

Public ownership of Raw material and final products
Including intermediates and fractions and...
processing waste

PDMPs coming from Italian plasma are used
in preference to commercial equivalents
(taking into account the therapeutic continuity of specific categories of patients)

PDMPs can be produced only from national plasma and
by authorised fractionation companies in EU plants

Regions, individually or in consortium, stipulate agreements
with authorised fractionation companies

The Italian Blood System and PDMPs - Relevant points

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The Italian Blood System and PDMPs - Authorised fractionation companies and plants/sites

Art. 15 (PDMPs production)

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April 12, 2012
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CSL Behring

Bern, *Gottingen, Marburg*

Grifols

Barcelona

Kedrion

Bolognana, *S. Antimo*

Octapharma

Stockholm, *Lingolsheim,
Springe, Dessau-Roßlau*

Takeda

Rieti, *Pisa, Wien, Lessines*

The Italian Blood System and PDMPs - Standard tender template 1/2

Art. 15 (PDMPs production)

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Ministerial Decrees
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Services requested in the tender

5.1) Pre-processing stage:

...

5.2) Plasma processing and production of blood products:

...

b) Production of at least the following blood products:

b1) Albumin;

b2) Polyvalent IGs for both intravenous and subcutaneous use;

...

5.3) distribution of blood products:

...

5.4) product safety:

...

}
↓
Yields +
Additional products

The Italian Blood System and PDMPs - Standard tender template 2/2

Art. 15 (PDMPs production)

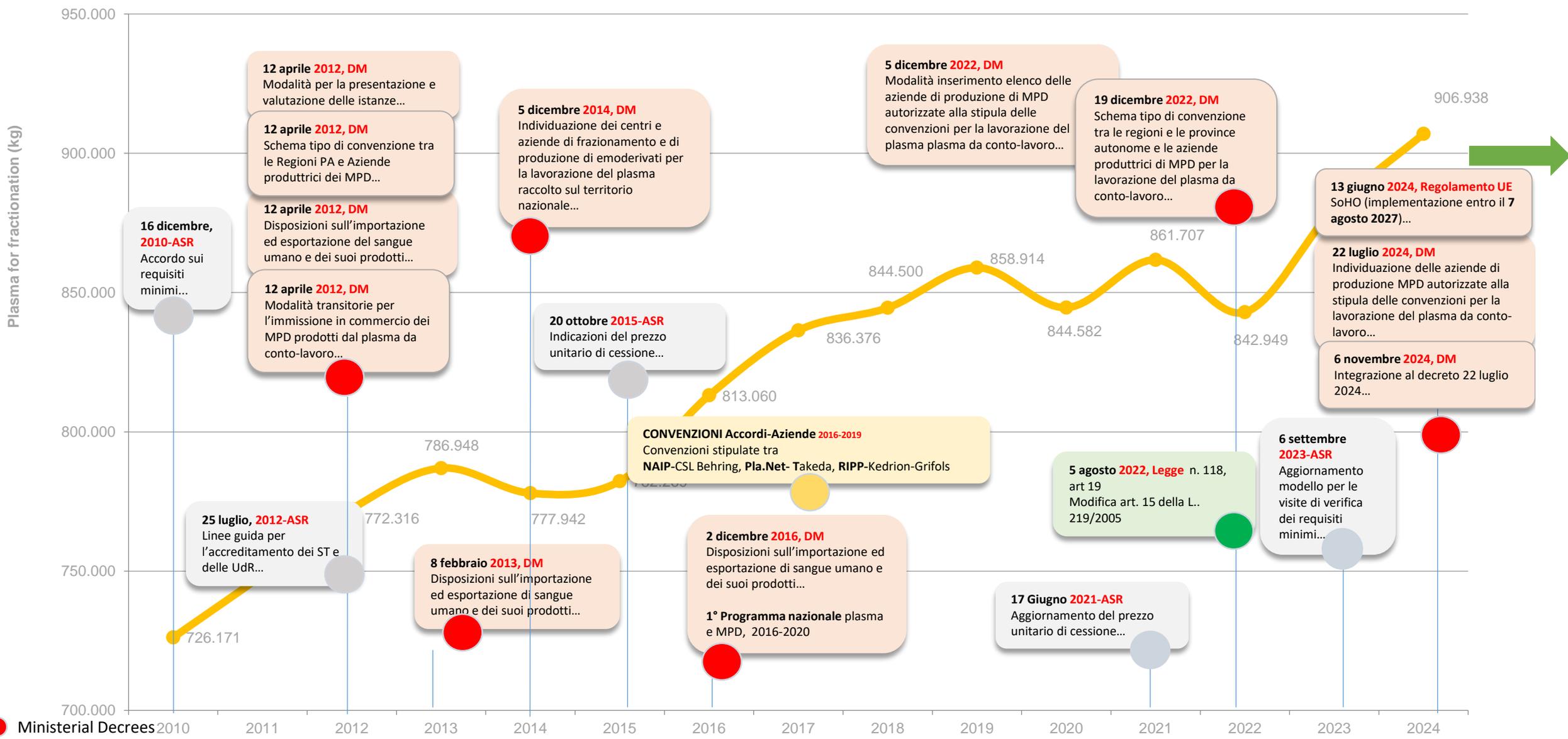
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Support for the improvement of QMS in

- a) plasma collection and production;
- b) monitoring systems;
- c) management aspects of the process;
- d) promotion of the appropriate use of PDMPs and research and development activities for new products and/or clinical indications, with particular reference to rare diseases;
- e) support for programmes and projects for the management of exceeding PDMPs

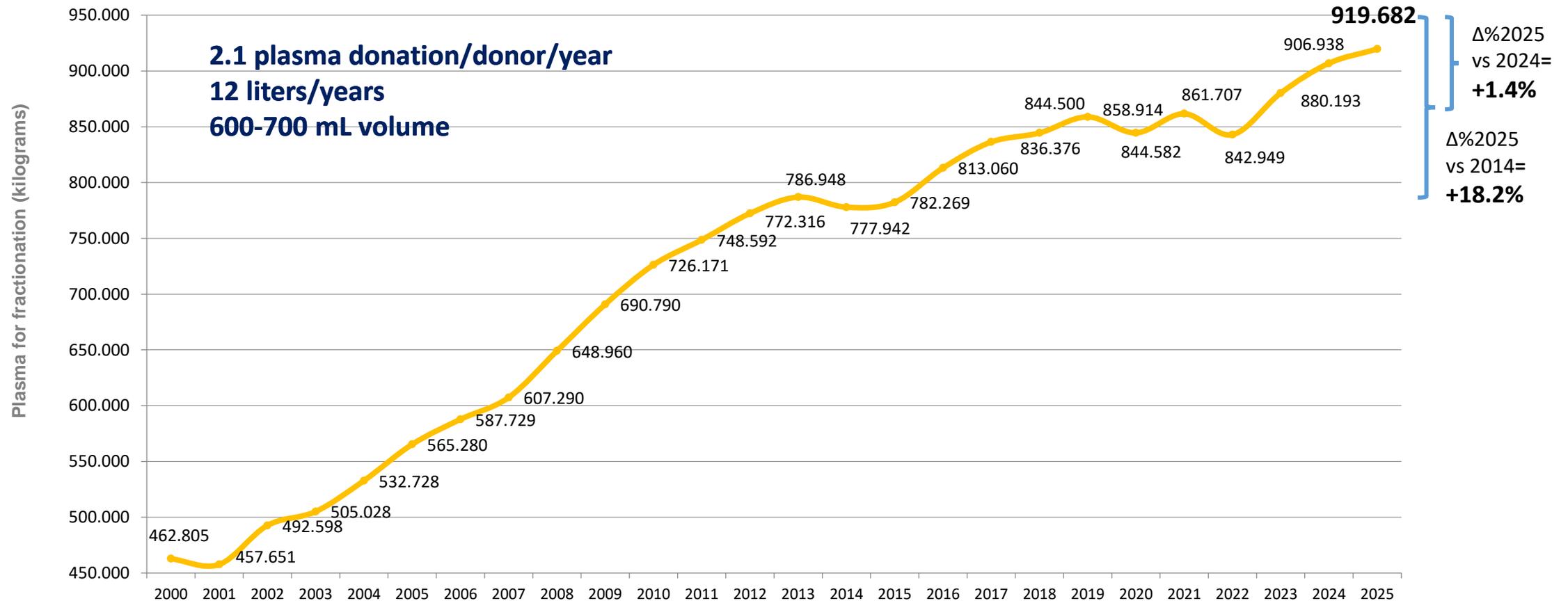
Regulatory and organisational developments



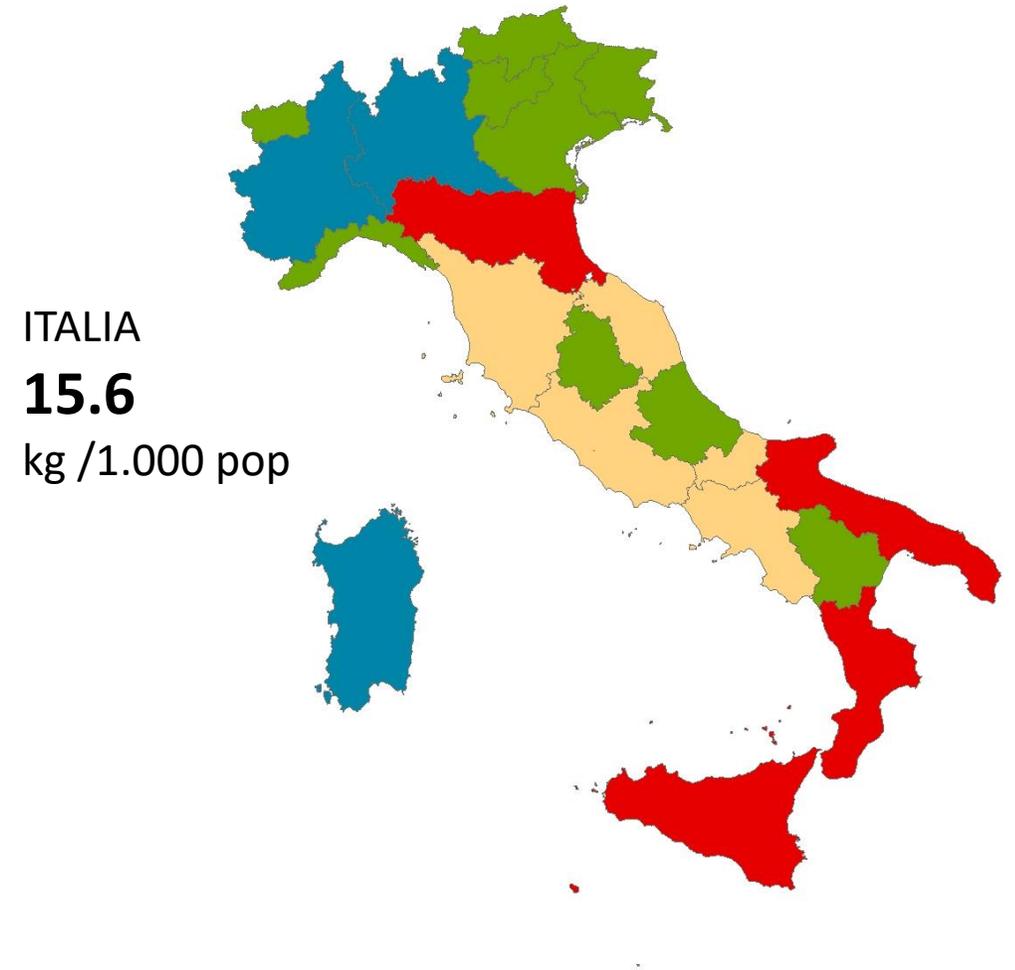
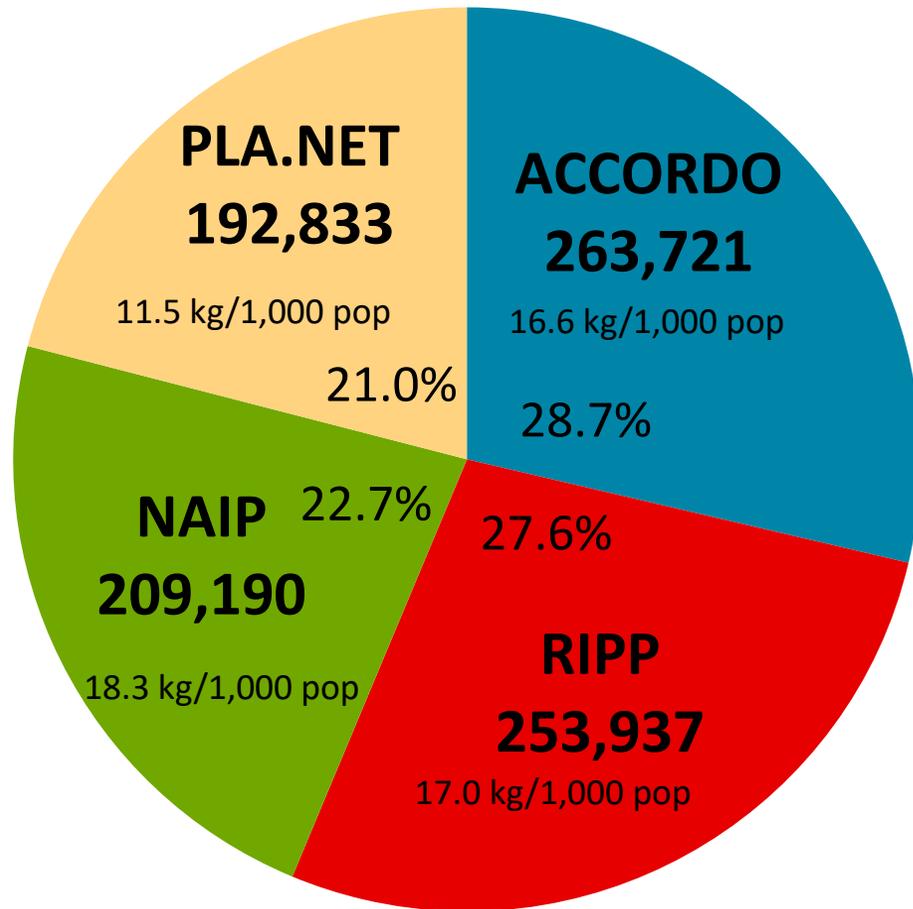
- Ministerial Decrees
- Law
- State-Regions Agreements

Part II

Plasma for fractionation 2000 - 2025 (total kilograms)



Toll fractionation System - Interregional Agreements - Year 2025



MARCH 2022

Four Regional Tenders for one Nation's Self Sufficiency

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Italian National Blood Centre
National Institute of Health, Rome

Interregional Agreements: summary of the Italian scenario 2022-2025

Four interregional Agreements:

-  NAIP
(New Interregional Agreement for PDMPs)
-  Accordo LPS
(Lombardy, Piedmont, Sardinia Agreement)
-  RIPP
(Plasma/Plasma-Derived Interregional Group)
-  Pla.Net
(Plasma Network)



Interregional Agreements: summary of the Italian scenario 2022-2025

CSL Behring

Albumin
 IVIg
 pdFVIII
 Fibrinogen (4,500 g)
 Ig-subcutaneous use
 FVIII/vWF (1,150 mln IUs)



NAIP

RIPP



Albumin
 IVIg
 pdFVIII
 pdFIX
 Antithrombin (40 mln IU)
 Ig-subcutaneous use
 3F-PCCs (18,5 mln IU)
 FVIII/vWF (8,5 mln IU)
 Alpha-1-proteinase inhibitor (3,500 mg)



Albumin
 IVIg
 pdFVIII
 aPCCs (5 mln FU)
 pdFIX (4 mln IU)
 Ig-subcutaneous use
 3F-PCCs (9 mln IU)
 4F-PCCs (2 mln IU)
 Protein C (500K IU)
 FVII (700K IU)
 FVIII/vWF (3 mln IU)



Pla.Net

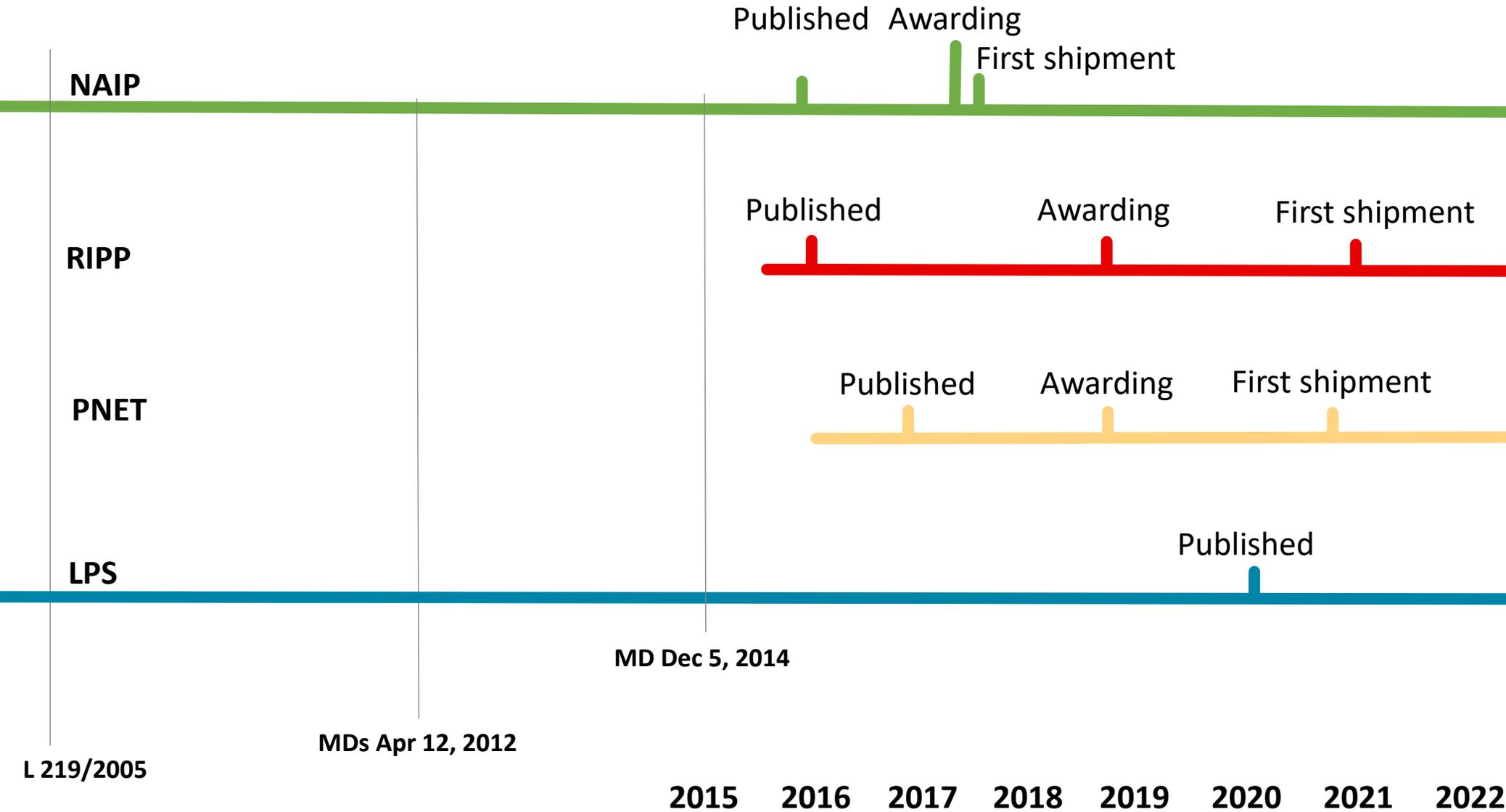


LPS

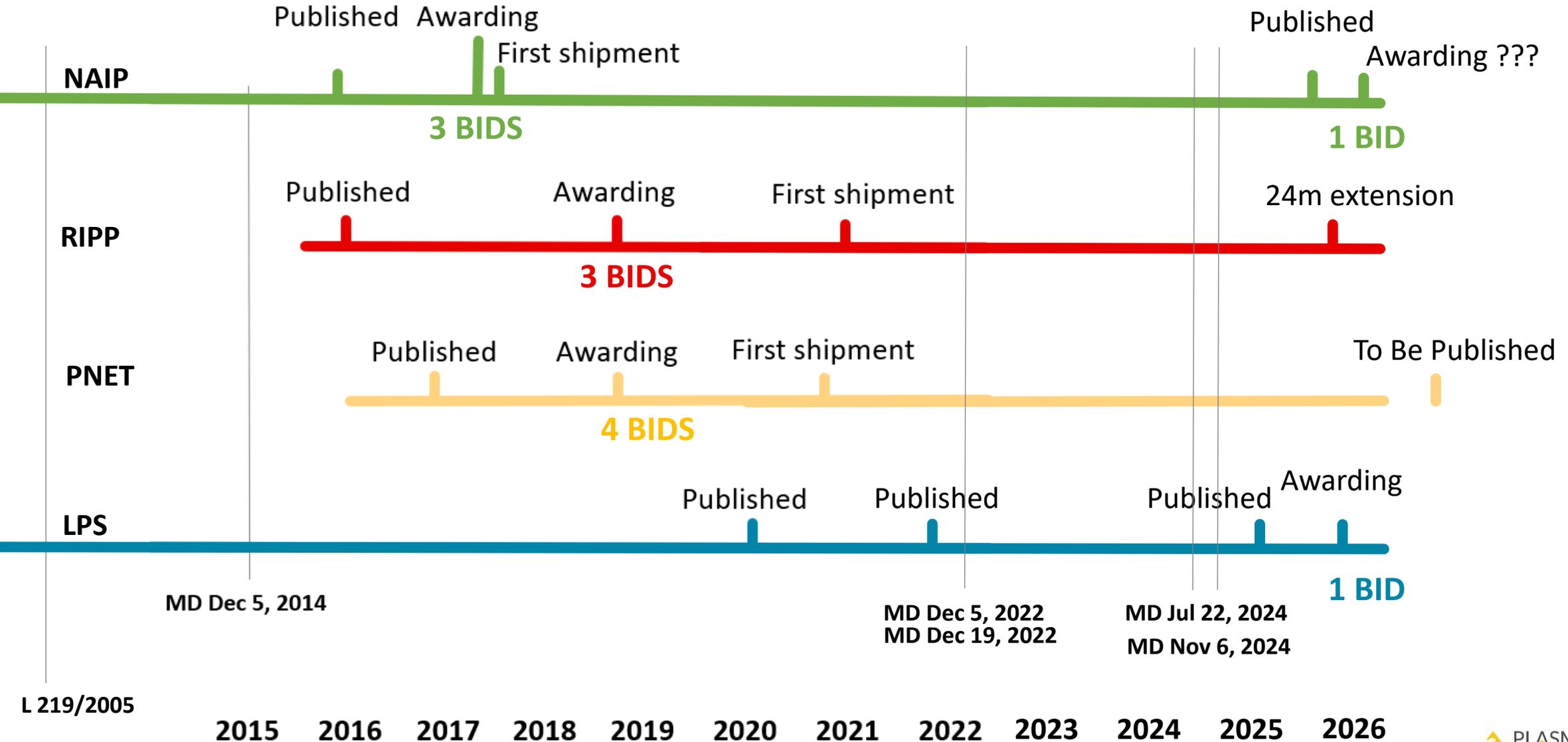
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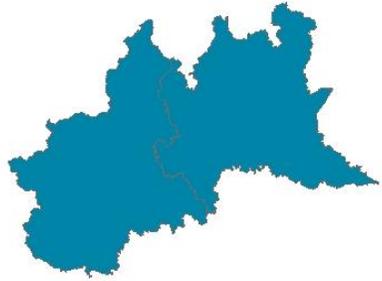
Timelines



Timelines



Interregional Tenders: scenario in 2025

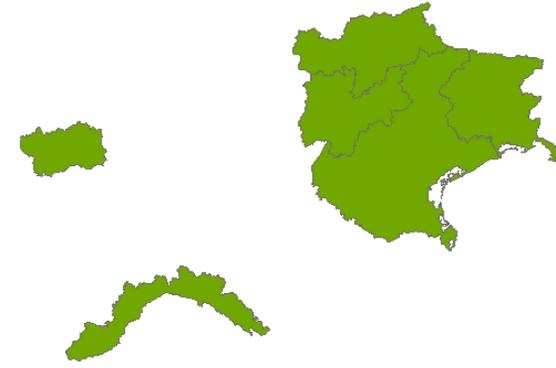


■ LPS

Pop. ≈16 mln

PfF ≈264,000 kg

16.6 kg/1,000 pop



■ NAIP

Pop. ≈20 mln

PfF ≈209,000 kg

18.3 kg/1,000 pop

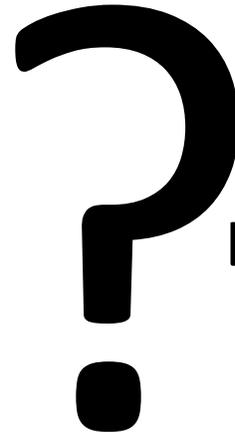


Pop.: Population
PfF: Plasma for Fractionation

Interregional Tenders: scenario in 2025



Leader: Lombardy Region
Published on June 2025
Pff: 236,000 kg
Length of the contract: 72 months
Starting Bid: \approx € 122 mln (VAT excl)
Quality : Price = 70 : 30



Leader: Veneto Region
Published on July 2025
Pff: \approx 200,000 kg
Length of the contract: 60 months + 48
Starting Bid: \approx € 126.8 mln (VAT excl)
Quality : Price = 75 : 25

1 BID

1 BID

Constraints?

Regulatory constraints

- Public ownership of the plasma, final products, intermediates, ...; (?)
- Separate processing cycle; (?)
- Complexity of the collection network in setting logistics;
- High burden of auditing sessions with impacts on PMF management

Tender constraints

- Long-term contracts and agreements with limited possibility of redefining the offer price;
- Penalising terms and conditions;
- Unbalanced bonus-malus clauses

Economic constraints

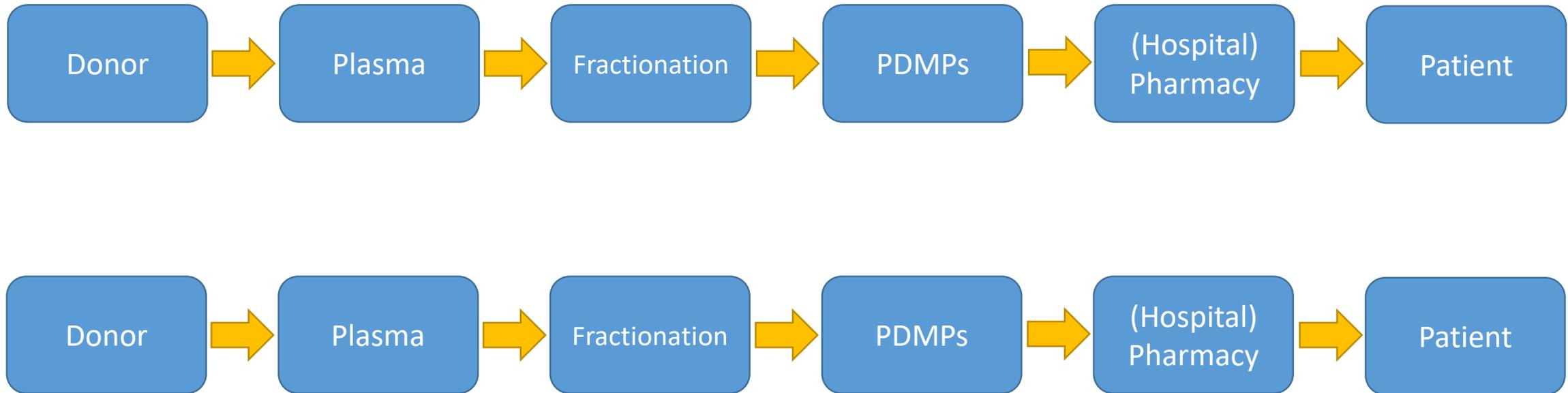
- “Unsustainable” starting bid
- Specific organisational shift for contract-manufacturing
- Processing national plasma vs commercial plasma

Competitiveness

Objectives of a Public health authority

- Monitor the commitments of all stakeholders on the Founding Principles of the System;
- Set the conditions so that the open market ensure the competition of the economic operators;
- Support the contracting authority with data and analysis and evidences (collection, demand, cost analysis, ...) in order to
- Ensure transparency in tender process (from the planning phase to the evaluation of the performance of the contract)

The plasma value chain(s)



no competition, but collaboration



PEACE, Please

