

# All roads lead to Rome

## Procuring and converting plasma in Europe

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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.

# All roads lead to Rome

...are you sure?!?

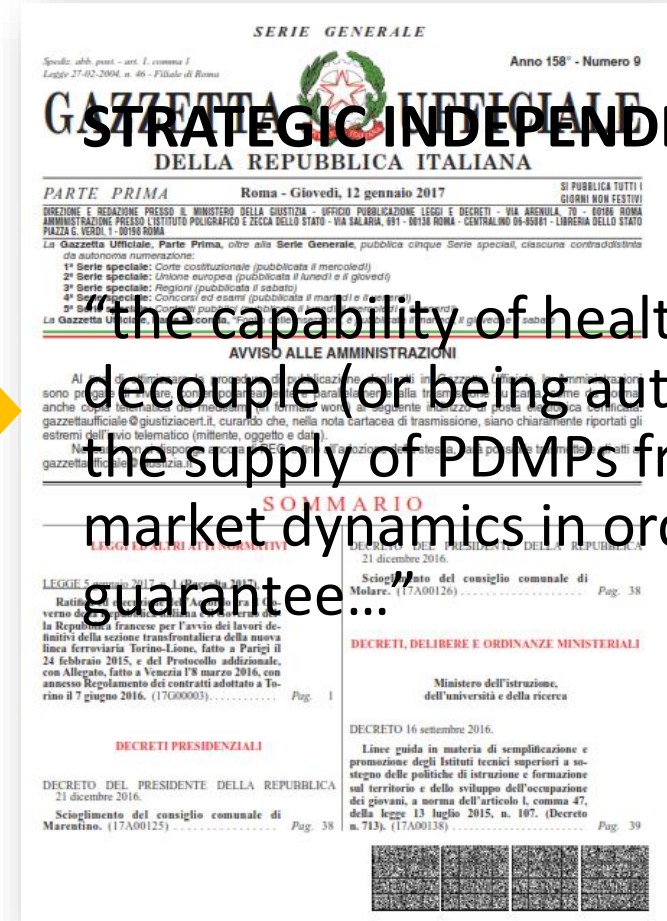
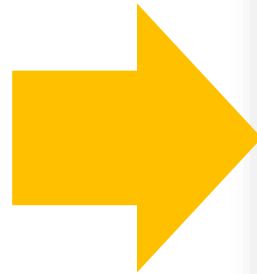


# Agenda

- Introduction
- Levels of collection of plasma for fractionation
- Manufacturing models and PDMPs return
- Demand for PDMPs and appropriateness
- Role of stakeholders

# Self-sufficiency in PDMPs 2.0

"[...] the ability to guarantee to patients, in a **systematic** and sustainable manner, the ready and **continuous availability** of a defined set of PDMPs with the highest degree of quality and safety and in accordance with the existing regulatory framework, meeting **appropriate clinical needs** through national plasma collection based on voluntary, non-remunerated donations with the contribution of market-acquired PDMPs."

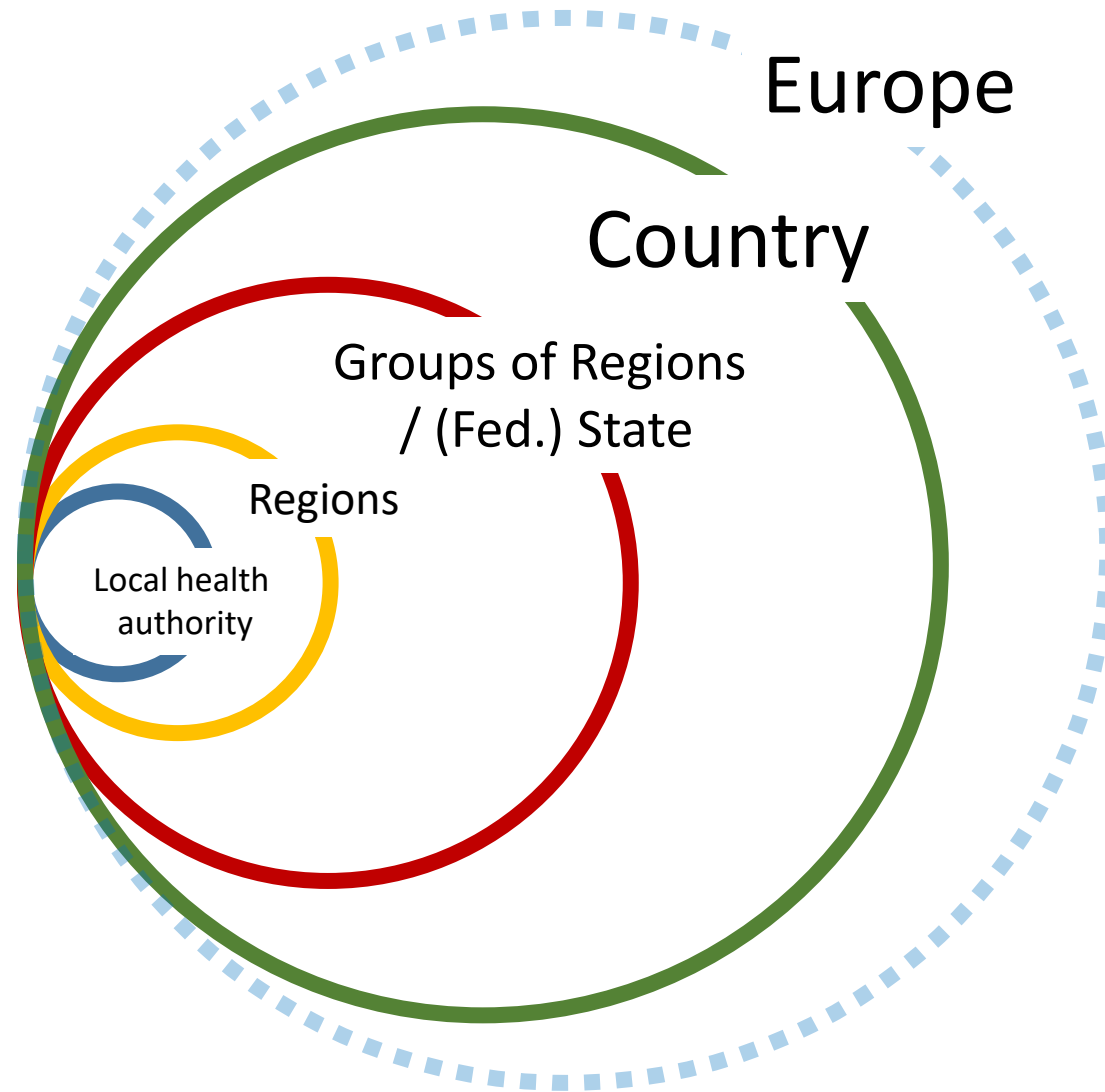


**STRATEGIC INDEPENDENCE**

“the capability of health systems to decouple (or being autonomous in) the supply of PDMPs from global market dynamics in order to guarantee...”

Systematic: a. made or arranged according to a system, method, or plan; regular; orderly; b. characterized by the use of method or orderly planning; methodical. Collins dictionary

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»



# Needs

How many patients do we need to treat with PDMPs in EU?

IG use related disorders

**NOT KNOWN**

a (c)rude estimate\* 100,000 - 400,000 + ...

Alpha-1-proteinase inhibitor deficiency

**NOT KNOWN**

a (c)rude estimate\* ~ 45,000 - 225,000

Von Willebrand Factor deficiency

**NOT KNOWN**

a (c)rude estimate\* ~ 45,000 - 225,000

\*OrphaNET prevalence rates for Primary immunodeficiency syndromes (PID); Secondary immunodeficiencies (SID); Primary Immune Thrombocytopenia (ITP); Guillain-Barré syndrome; Kawasaki Disease; Chronic Inflammatory Demyelinating Polyradiculoneuropathy (CIDP); Multifocal motor neuropathy (MMN); Alpha-1-proteinase inhibitor deficiency; Von Willebrand Factor deficiency

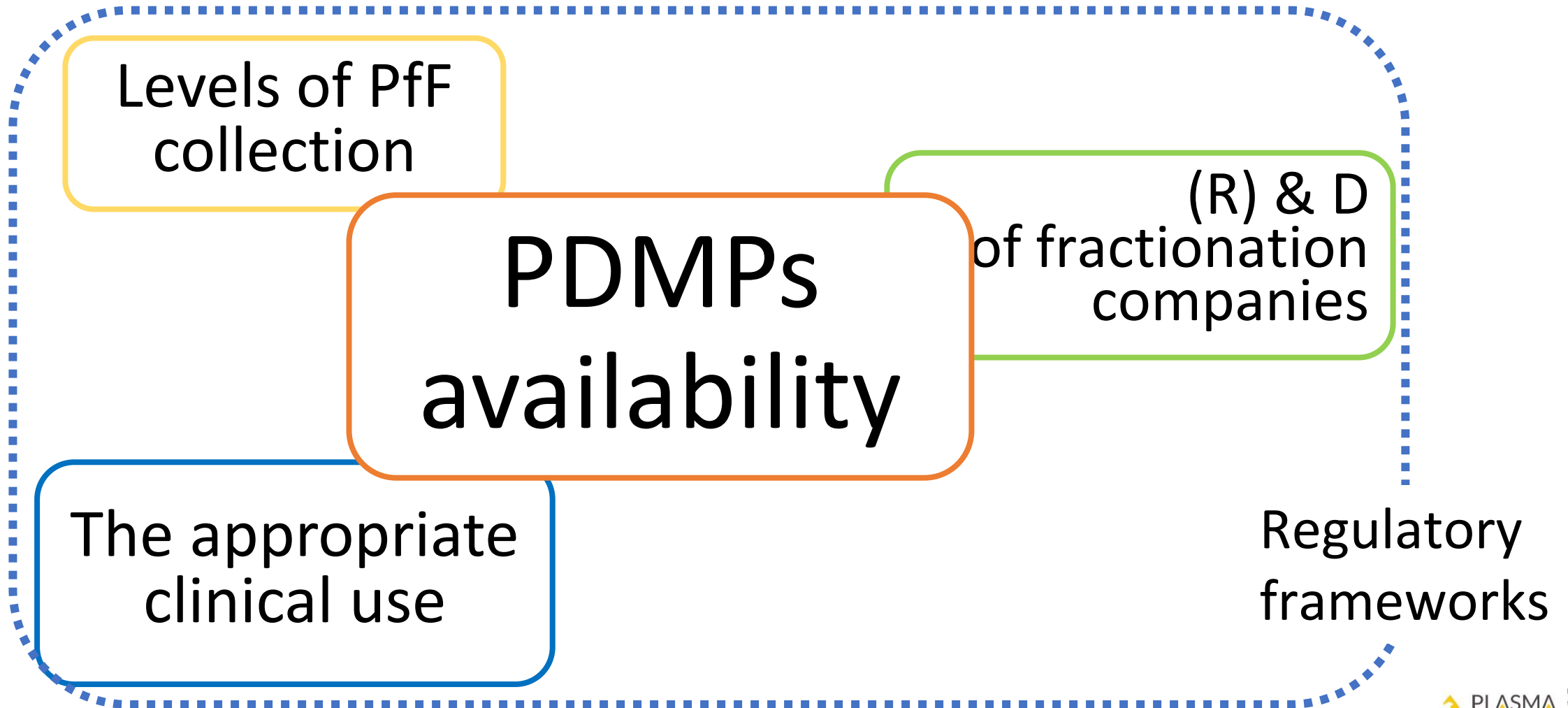
# Needs

Registers...?

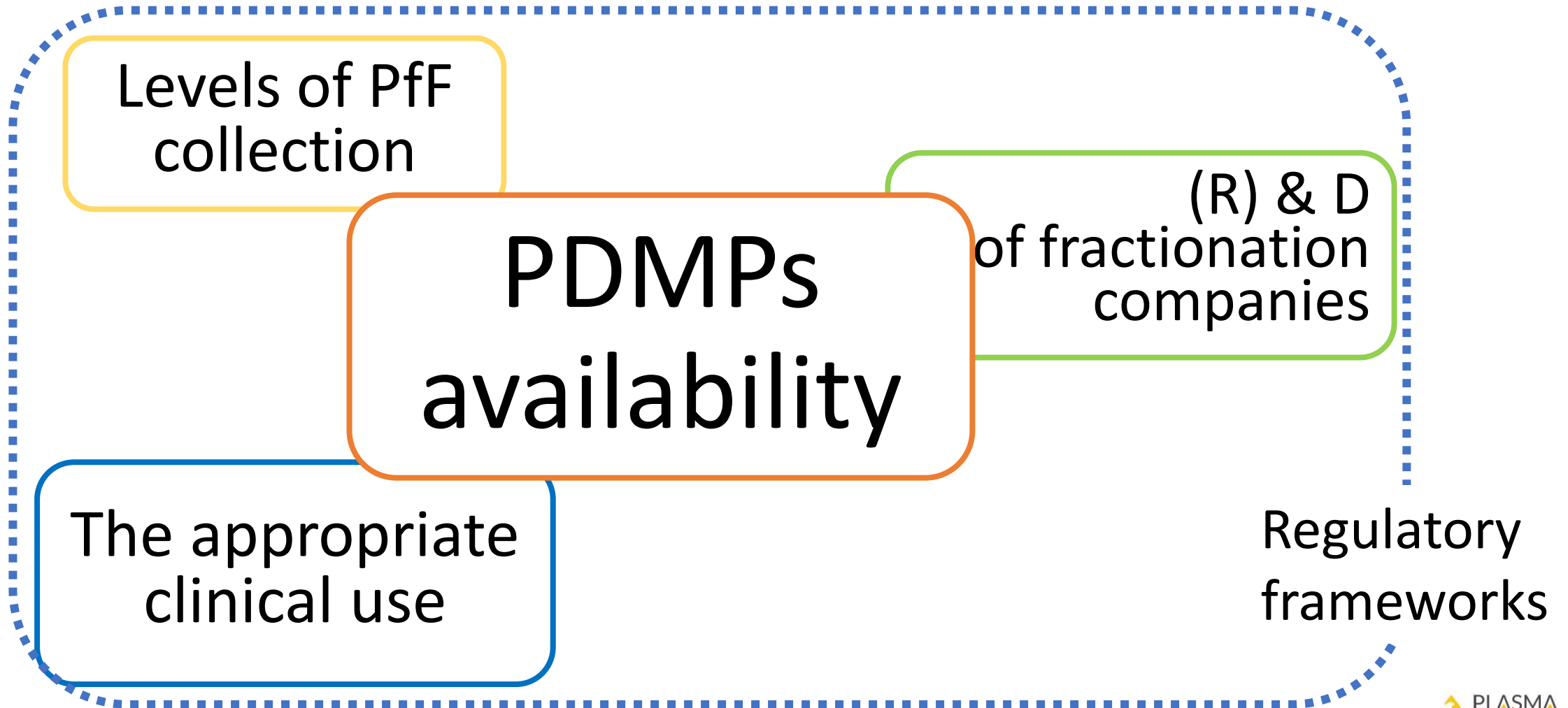
(probably) The most effective strategy to evaluate the needs is to monitor the demand for PDMPs using ATC classification or even specific marketing authorisation codes (pdFVIII vs rFVIII or SCIg vs SC/IMIg or IVIg vs HtIVIg) accessing data from pharma competent authorities (or MoH) in order to perform analysis at different time-space dimensions levels.

For albumin and (above all) Ig cross-references with the in-label clinical indications is desired

# (main) factors influencing the availability of PDMPs



# (main) factors influencing the availability of PDMPs



# WP4 - SUPPLY PROJECT

## Ultimate goal

To formulate recommendations for the development of a proposal of common EU policies (or also legal framework) aimed to support national and EU efforts to achieve a higher degree of strategic independence from non-EU sources in the collection of plasma and its fractionation in PDMPs

Gain clear insight into the current European national policies/legal frameworks for a) the strategic independence in collection of plasma for fractionation b) the management of PDMPs coming from national plasma collection.

Assess the national demand for PDMPs, including pharmaceutical expenditure

Assess the national needs of plasma for fractionation.

Identify and compare the different tendering models for the choice of the fractionator.

Gain a clear understanding and description of the state-of-the art of plasma economics which can be useful and educational for BEs in their interaction with the fractionators.

## **WP4. National and EU infrastructures / policy/legal framework for plasma collection and PDMPs supply**

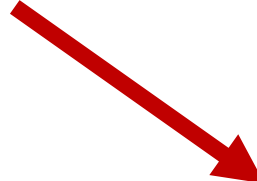
- Task 4.1 Survey on plasma collection and PDMPs production from national plasma in EU
- Task 4.2 Report on Analysis of policies and/or legal frameworks in plasma collection and PDMPs management
- Task 4.3 Report on Data & Tools for plasma collection and PDMPs management
- Task 4.4 Position paper on Distribution of PDMPs coming from EU/national plasma
- Task 4.5 Report on Plasma/PDMPs economics and tenders
- Task 4.6 Develop recommendations

## **TASK 4.1 SURVEY on *Plasma collection and PDMPs production from national plasma in EU***

### **OBJECTIVES**

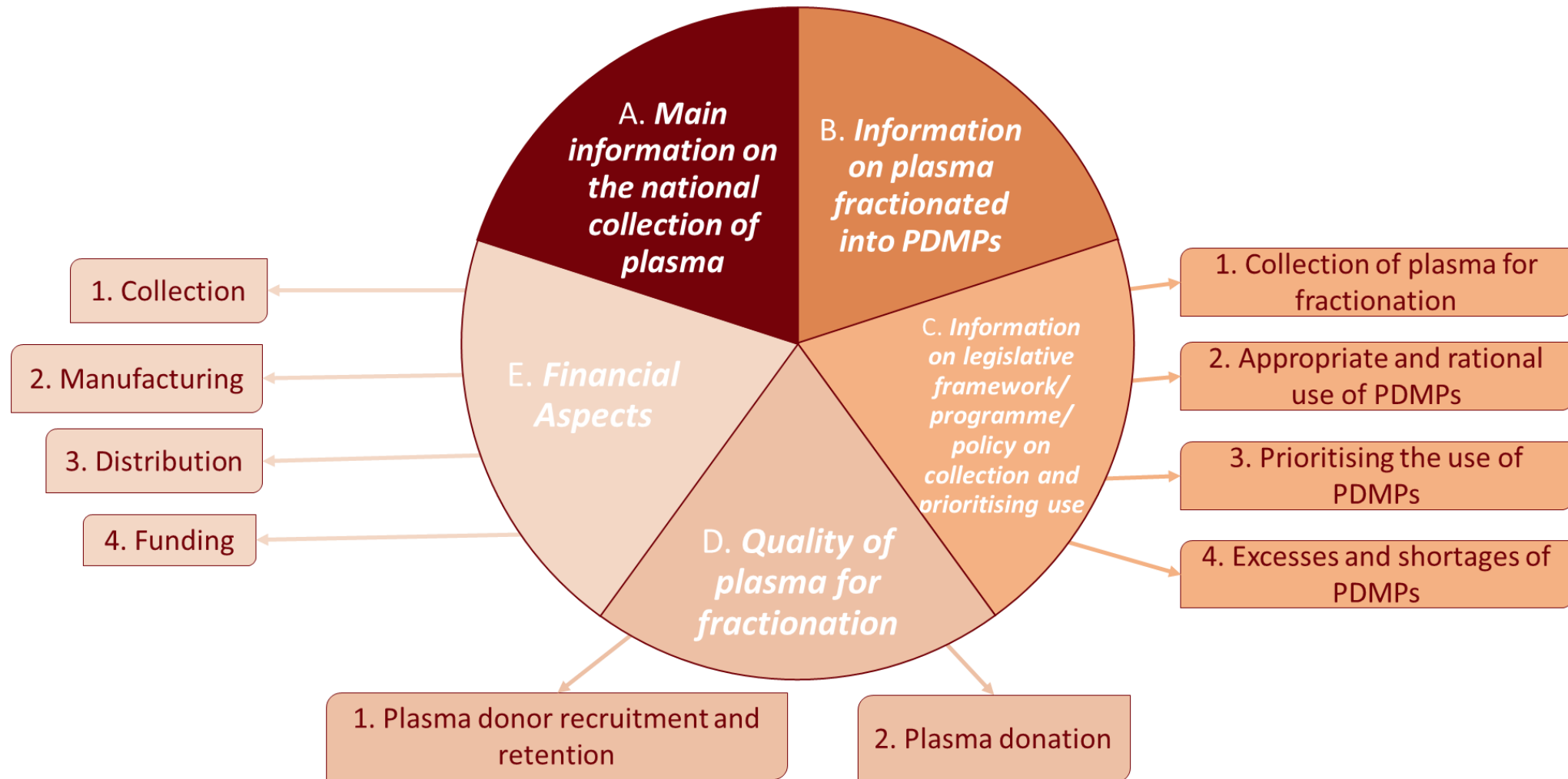


Investigate the presence and the effectiveness of different national legislation/policies aimed at promoting strategic independence in the public sector for PDMPs coming from national plasma.



Define the framework capable to mitigate the effects of the decrease in plasma availability (and consequently of PDMPs on the market) reported by pharmaceutical companies following the Covid-19 pandemic and, in general, in any crisis of plasma supply from outside Europe.

# TASK 4.1 SURVEY Sections

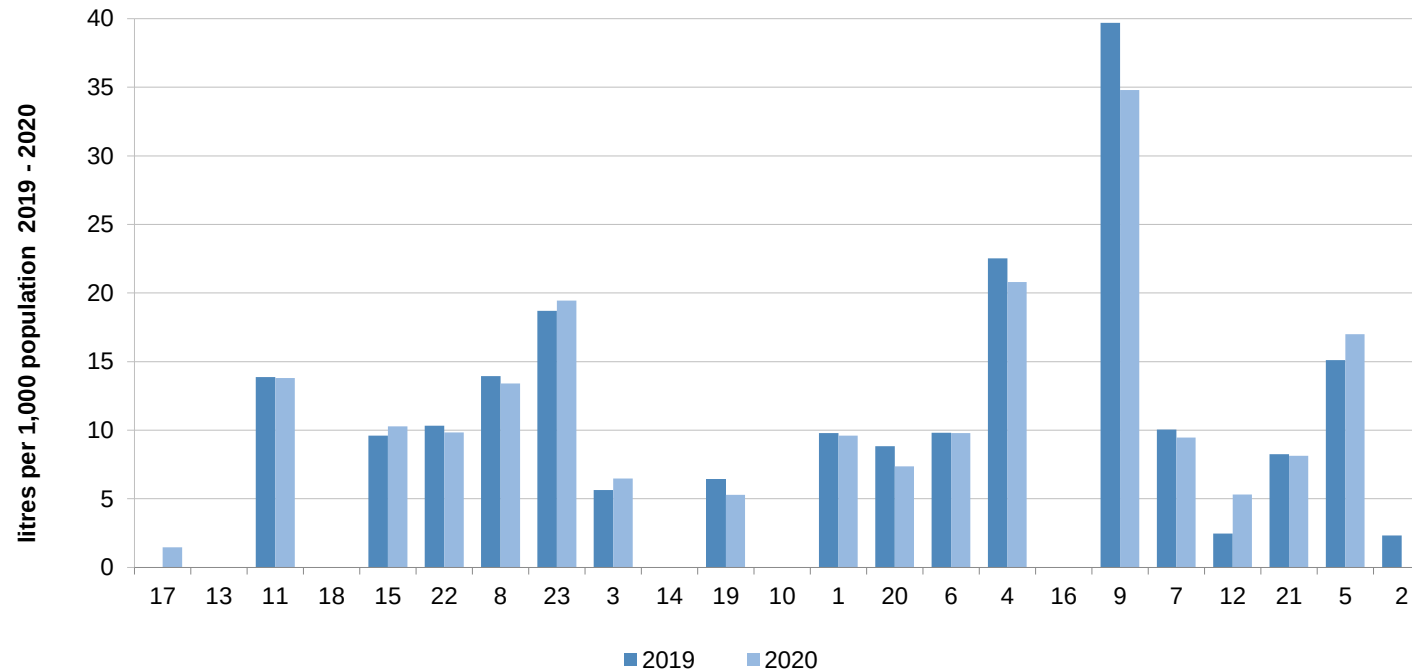


## Section A. Main information on the national collection of plasma

### Q3 - Volumes collected by public sector

#### Public sector

#### Fractionation

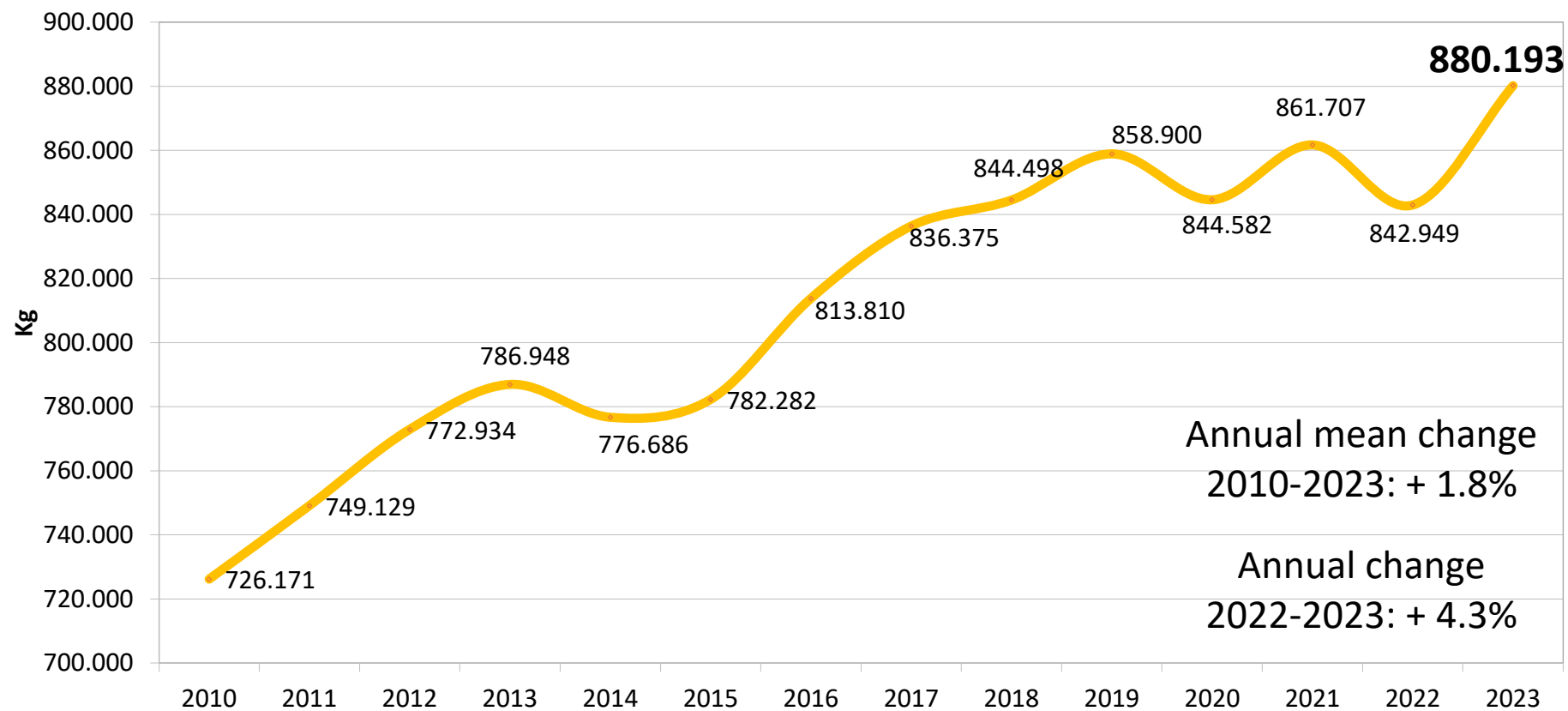


2020 range: 1.5 - 34.8

2019: 15.6 kg 1,000 pop

2020: 14.5 kg 1,000 pop

# Plasma for fractionation (kg) 2010-2023



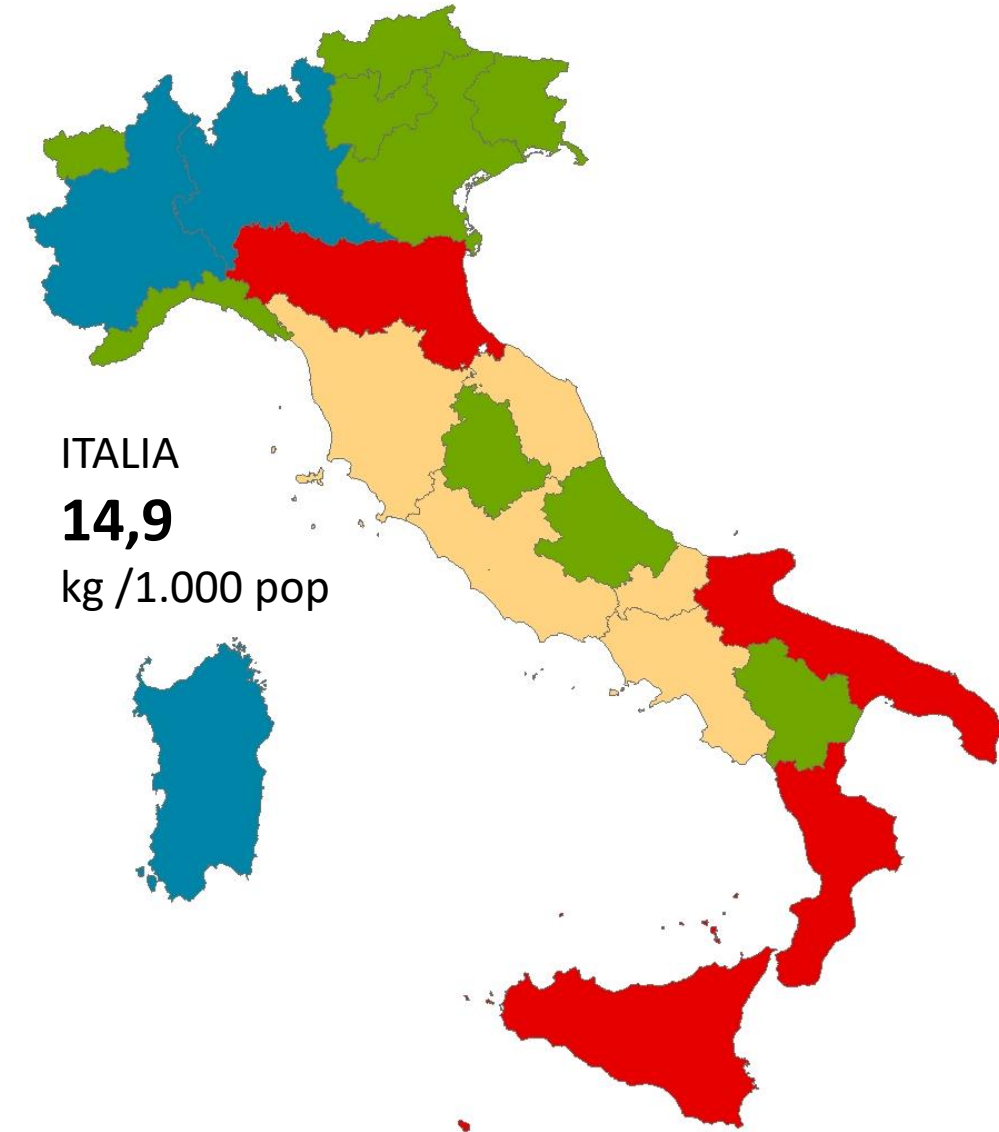
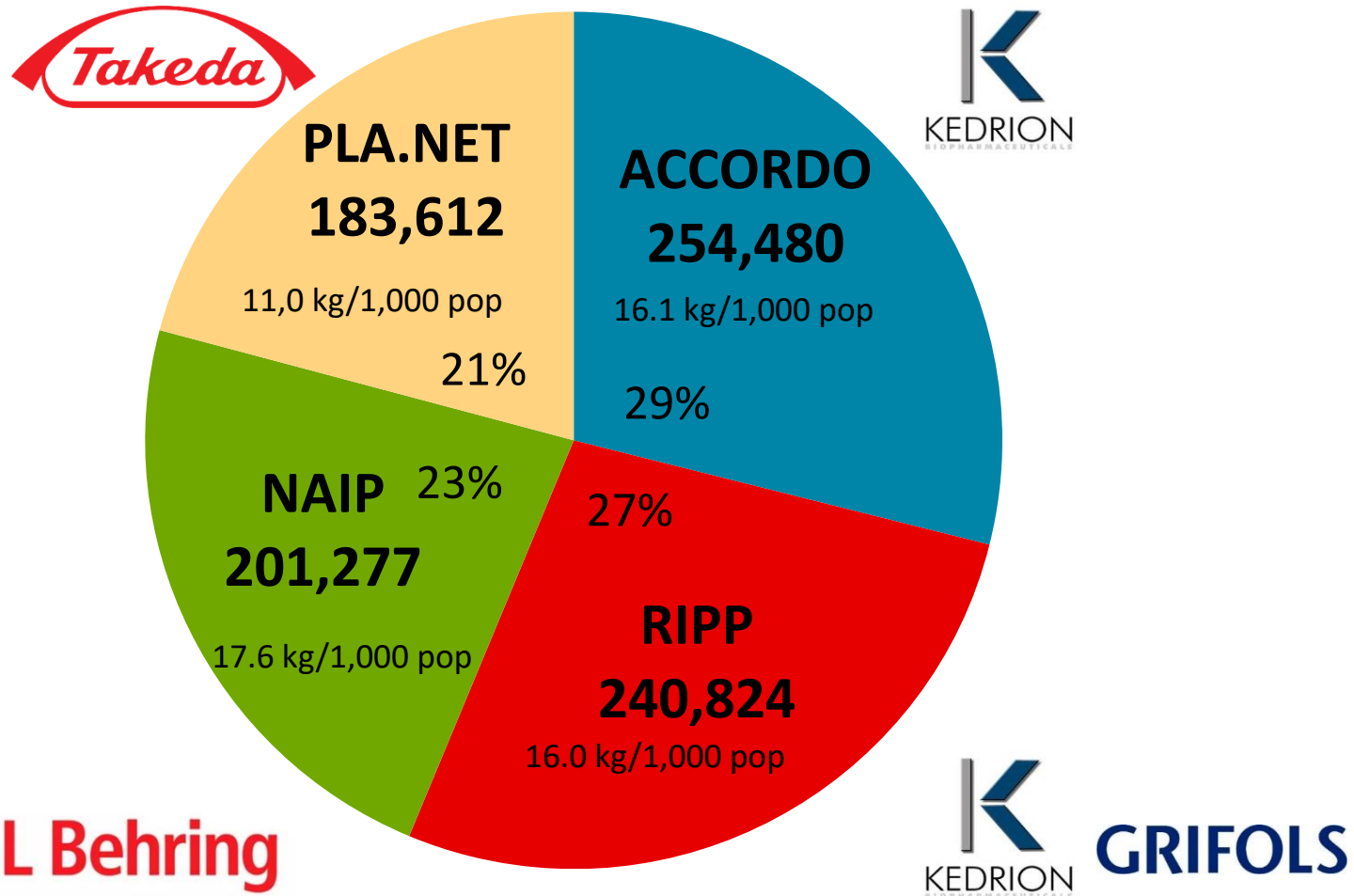
# PLASMA PER FRAZIONAMENTO CONFERITO ALLA LAVORAZIONE INDUSTRIALE (kg): ANNI 2022-2023

| REGIONI, PP AA,<br>Ministero Difesa | CATEGORIA A |         |       | CATEGORIA B |          |       | CATEGORIA C |         |       | TOTALE  |         |       |
|-------------------------------------|-------------|---------|-------|-------------|----------|-------|-------------|---------|-------|---------|---------|-------|
|                                     | 2022        | 2023    | %     | 2022        | 2023     | %     | 2022        | 2023    | %     | 2022    | 2023    | %     |
| Valle d'Aosta                       | 1.073       | 1.102   | 2,8   | 1.454       | 1.330    | -8,5  | -           | -       | NA    | 2.527   | 2.432   | -3,7  |
| Piemonte                            | 22.676      | 25.080  | 10,6  | 46.717      | 48.410   | 3,6   | 1.988       | 2.059   | 3,5   | 71.381  | 75.549  | 5,8   |
| Liguria                             | 5.934       | 6.783   | 14,3  | 18.009      | 18.278   | 1,5   | -           | -       | NA    | 23.943  | 25.061  | 4,7   |
| Lombardia                           | 46.259      | 51.390  | 11,1  | 99.616      | 99.208   | -0,4  | 9.107       | 9.073   | -0,4  | 154.982 | 159.671 | 3,0   |
| Prov. Auton. di Trento              | 680         | 1.342   | 97,4  | 6.599       | 6.796    | 3,0   | -           | -       | NA    | 7.279   | 8.138   | 11,8  |
| Prov. Auton. di Bolzano             | 2.038       | 2.556   | 25,4  | 5.906       | 5.652    | -4,3  | -           | -       | NA    | 7.944   | 8.208   | 3,3   |
| Friuli Venezia Giulia               | 13.975      | 13.976  | 0,0   | 14.579      | 14.761   | 1,2   | 26          | 119     | 347,8 | 28.581  | 28.855  | 1,0   |
| Veneto                              | 26.339      | 29.076  | 10,4  | 56.992      | 58.870   | 3,3   | 4.731       | 4.949   | 4,6   | 88.061  | 92.896  | 5,5   |
| Emilia-Romagna                      | 40.380      | 43.693  | 8,2   | 53.670      | 53.077   | -1,1  | 2.224       | 3.007   | 35,2  | 96.274  | 99.777  | 3,6   |
| Toscana                             | 23.204      | 25.065  | 8,0   | 40.772      | 39.980   | -1,9  | -           | -       | NA    | 63.976  | 65.045  | 1,7   |
| Umbria                              | 1.609       | 1.916   | 19,0  | 8.490       | 8.947    | 5,4   | -           | -       | NA    | 10.099  | 10.862  | 7,6   |
| Marche                              | 15.193      | 16.496  | 8,6   | 19.452      | 19.010   | -2,3  | -           | -       | NA    | 34.645  | 35.506  | 2,5   |
| Lazio                               | 4.338       | 5.423   | 25,0  | 34.824      | 37.200   | 6,8   | 5.174       | 4.751   | -8,2  | 44.336  | 47.374  | 6,9   |
| Sardegna                            | 568         | 517     | -9,0  | 18.140      | 18.454   | 1,7   | 153         | 289     | 88,6  | 18.861  | 19.260  | 2,1   |
| Abruzzo                             | 4.786       | 4.857   | 1,5   | 13.411      | 12.865   | -4,1  | 152         | 117     | -23,2 | 18.349  | 17.839  | -2,8  |
| Campania                            | 665         | 622     | -6,5  | 27.469      | 30.179   | 9,9   | 959         | 849     | -11,4 | 29.093  | 31.650  | 8,8   |
| Molise                              | 290         | 875     | 202,2 | 2.981       | 2.899    | -2,7  | -           | -       | NA    | 3.270   | 3.774   | 15,4  |
| Puglia                              | 6.870       | 8.474   | 23,3  | 40.011      | 41.823   | 4,5   | 942         | 1.021   | 8,5   | 47.823  | 51.318  | 7,3   |
| Basilicata                          | 1.458       | 1.940   | 33,1  | 4.015       | 3.335    | -16,9 | 1.293       | 1.712   | 32,5  | 6.765   | 6.987   | 3,3   |
| Calabria                            | 1.360       | 2.421   | 77,9  | 17.250      | 17.344   | 0,5   | 9           | 5       | -46,1 | 18.620  | 19.770  | 6,2   |
| Sicilia                             | 17.046      | 19.128  | 12,2  | 50.084      | 50.816   | 1,5   | 10          | 15      | 55,2  | 67.139  | 69.960  | 4,2   |
| Ministero Difesa                    | -           | -       | NA    | 159         | 140      | -12,3 | 157         | 123     | -21,5 | 316     | 262     | -16,8 |
| ITALIA                              | 236.739     | 262.732 | 11,0  | 580.598     | 589.372* | 1,5   | 26.925      | 28.090* | 4,3   | 844.263 | 880.193 | 4,3   |

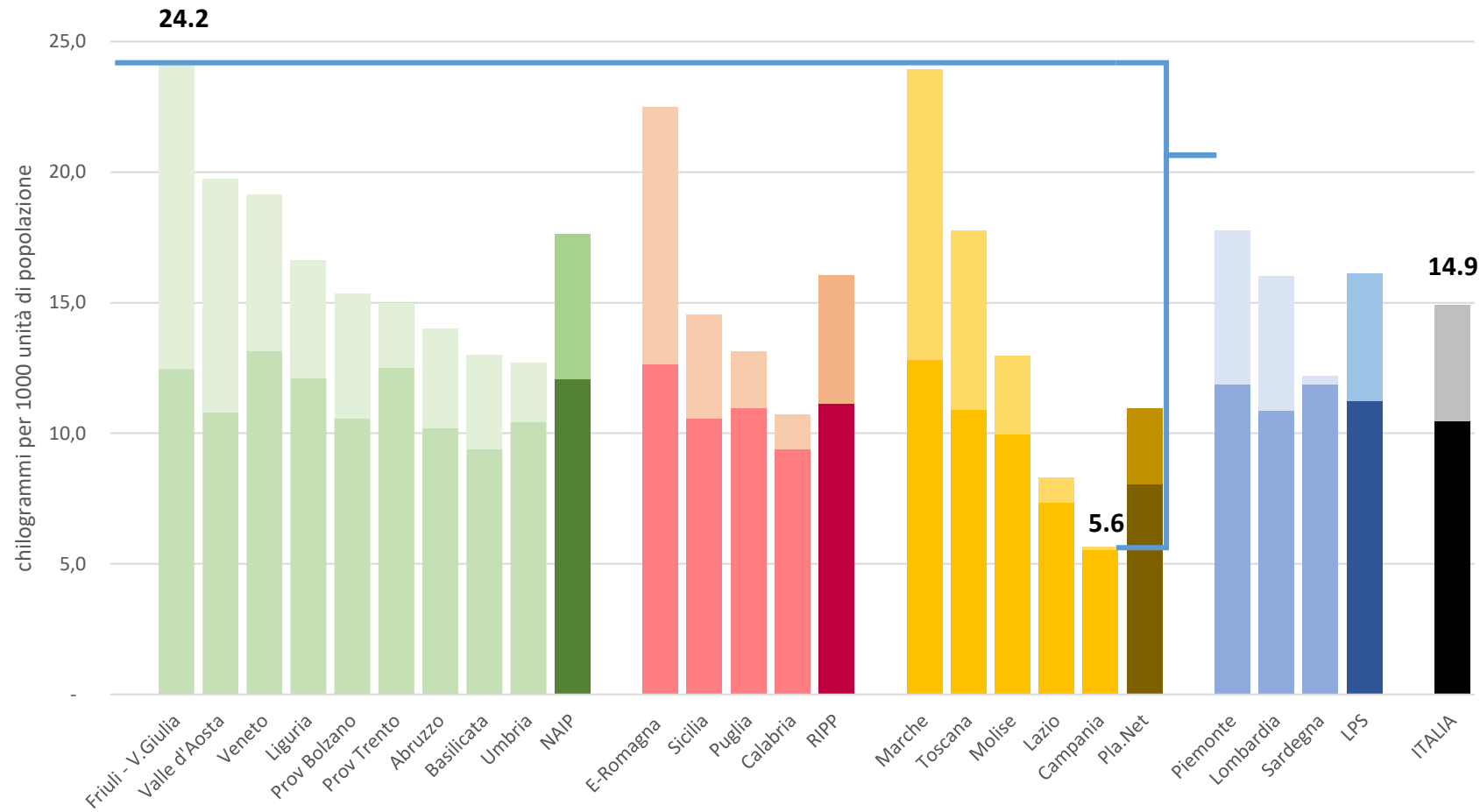
\* Dato soggetto a lievi variazioni

Data sources: - Adapted by the Italian National Blood Centre on data from Fractionation industries. January 2024

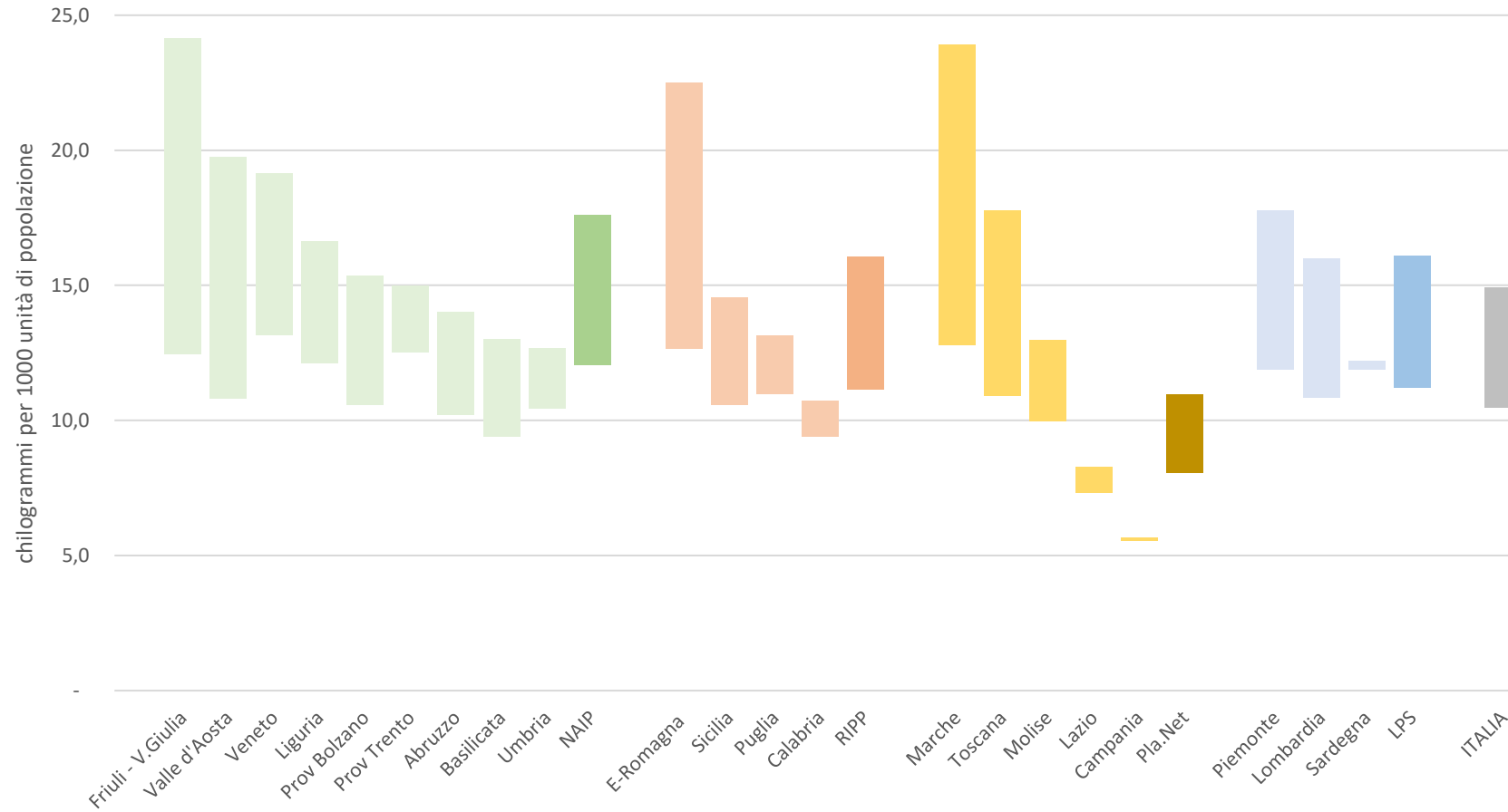
# ACCORDI INTERREGIONALI PER IL SISTEMA DI PRODUZIONE DEI MPD PLASMA PER FRAZIONAMENTO 2023



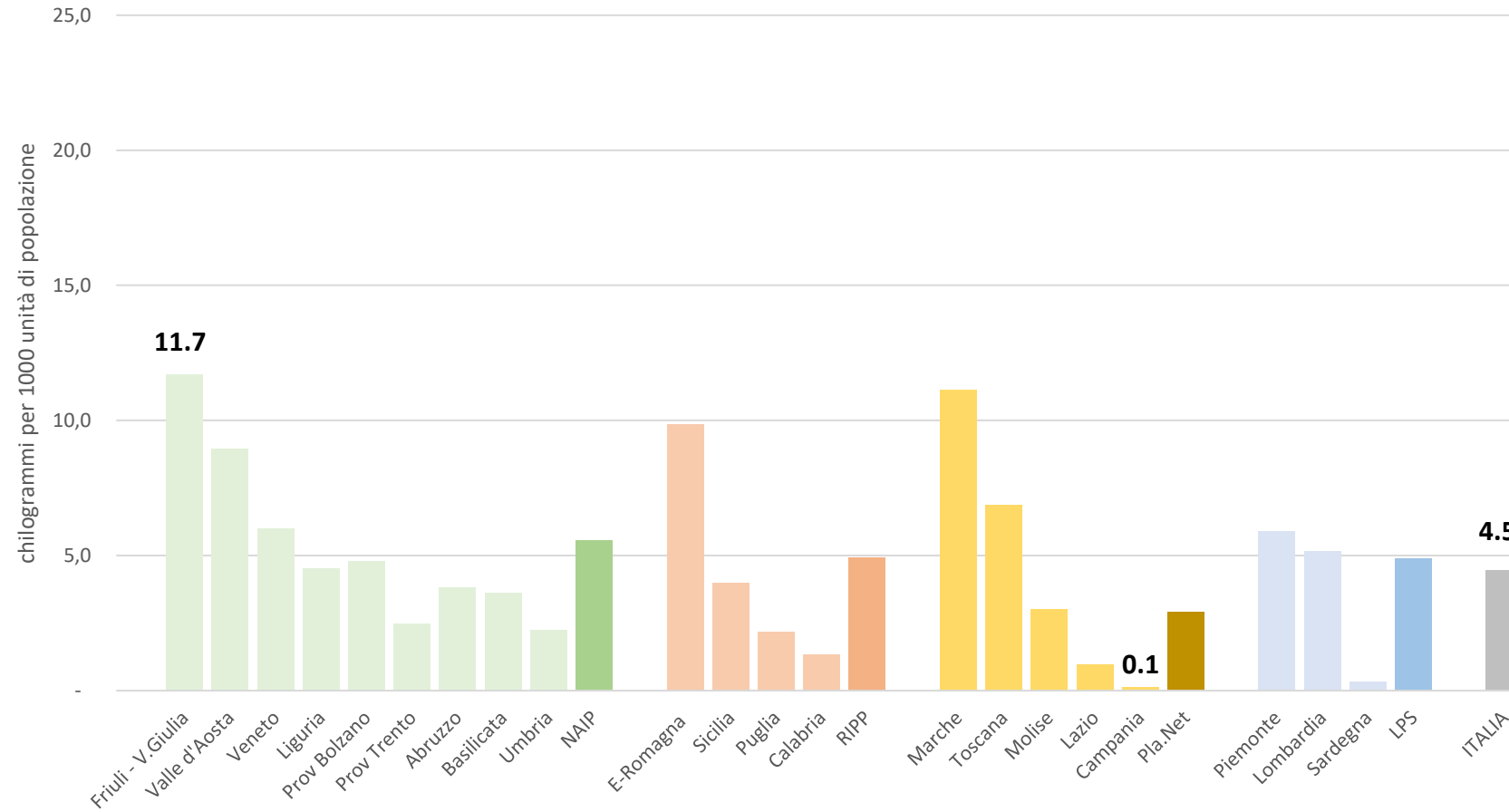
# PLASMA PER FRAZIONAMENTO per REGIONE, PPAA, ACCORDO, CATEGORIA . Anno 2023 (kg/1.000 pop)



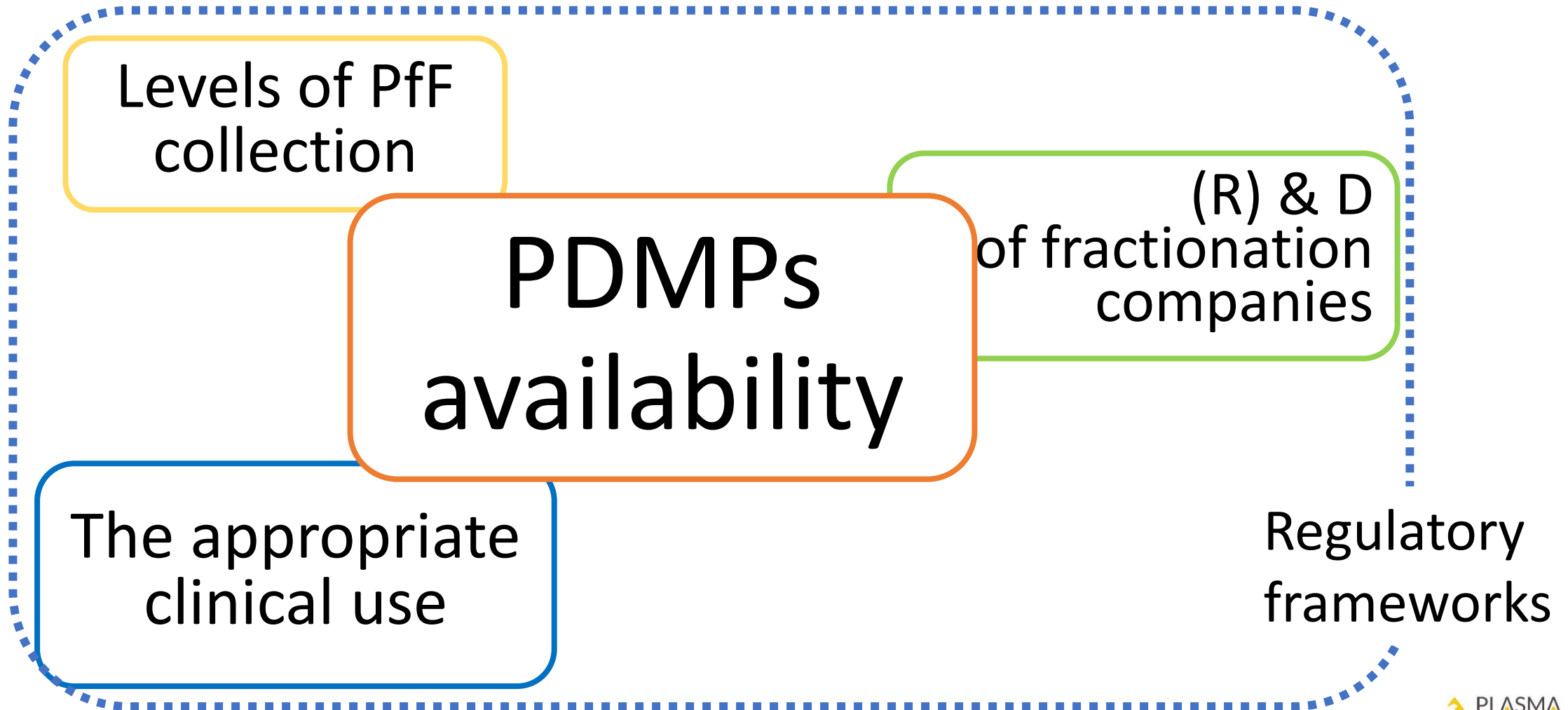
# PLASMA PER FRAZIONAMENTO per REGIONE, PPAA, ACCORDO, CATEGORIA A. Anno 2023 (kg/1.000 pop)



# PLASMA PER FRAZIONAMENTO per REGIONE, PPAA, ACCORDO, CATEGORIA A. Anno 2023 (kg/1.000 pop)



# (main) factors influencing the availability of PDMPs



## Section B.

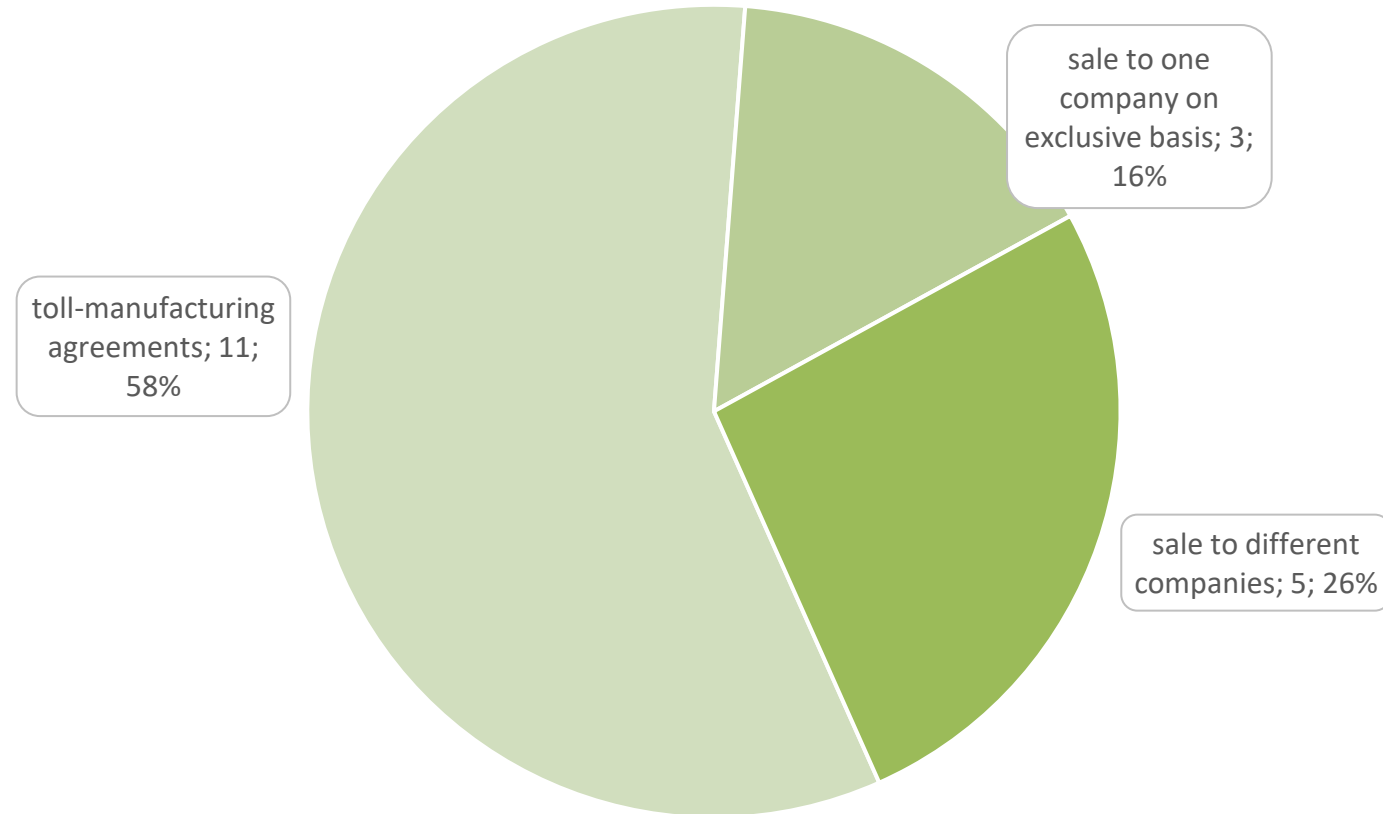
### Information on plasma fractionated into PDMPs

## Section B. Information on plasma fractionated into PDMPs

### Q8 - Fractionation framework

Q8

19/19 Answers

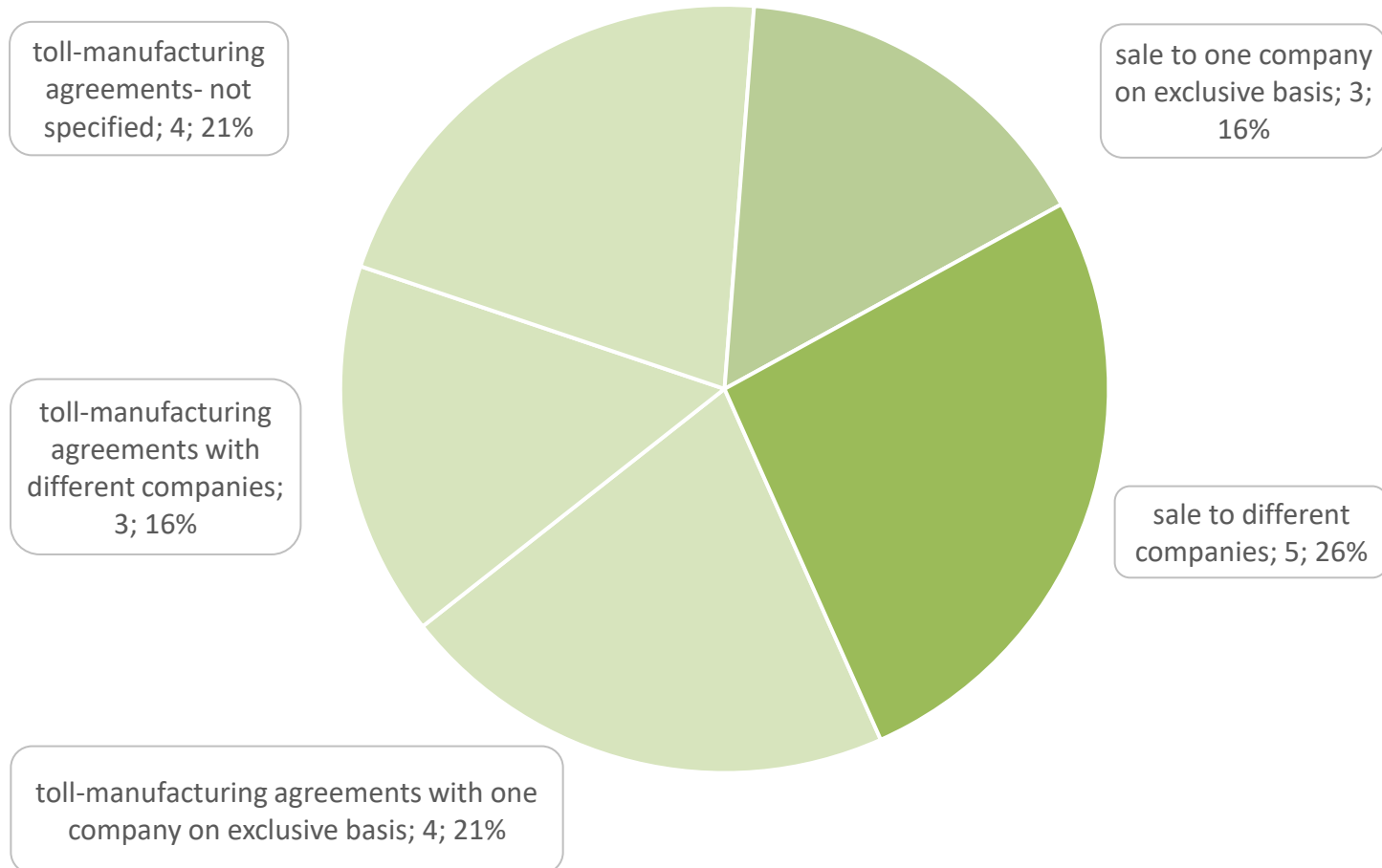


## Section B. Information on plasma fractionated into PDMPs

### Q8 - Fractionation framework

Q8

19/19 Answers

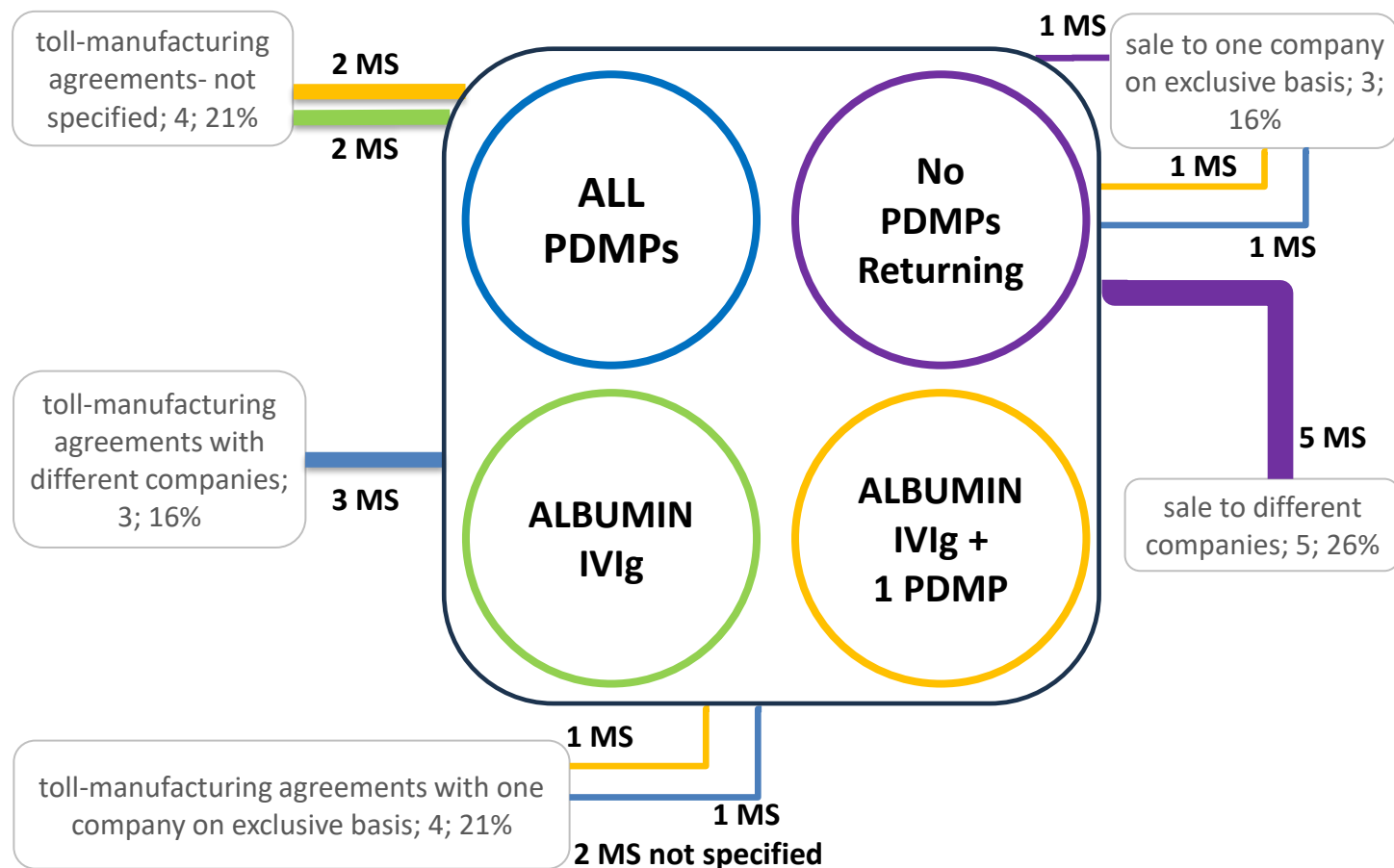


## Section B. Information on plasma fractionated into PDMPs

### Q9 - PDMPs returning

Q9

19/19 Answers



## Section B. Information on plasma fractionated into PDMPs

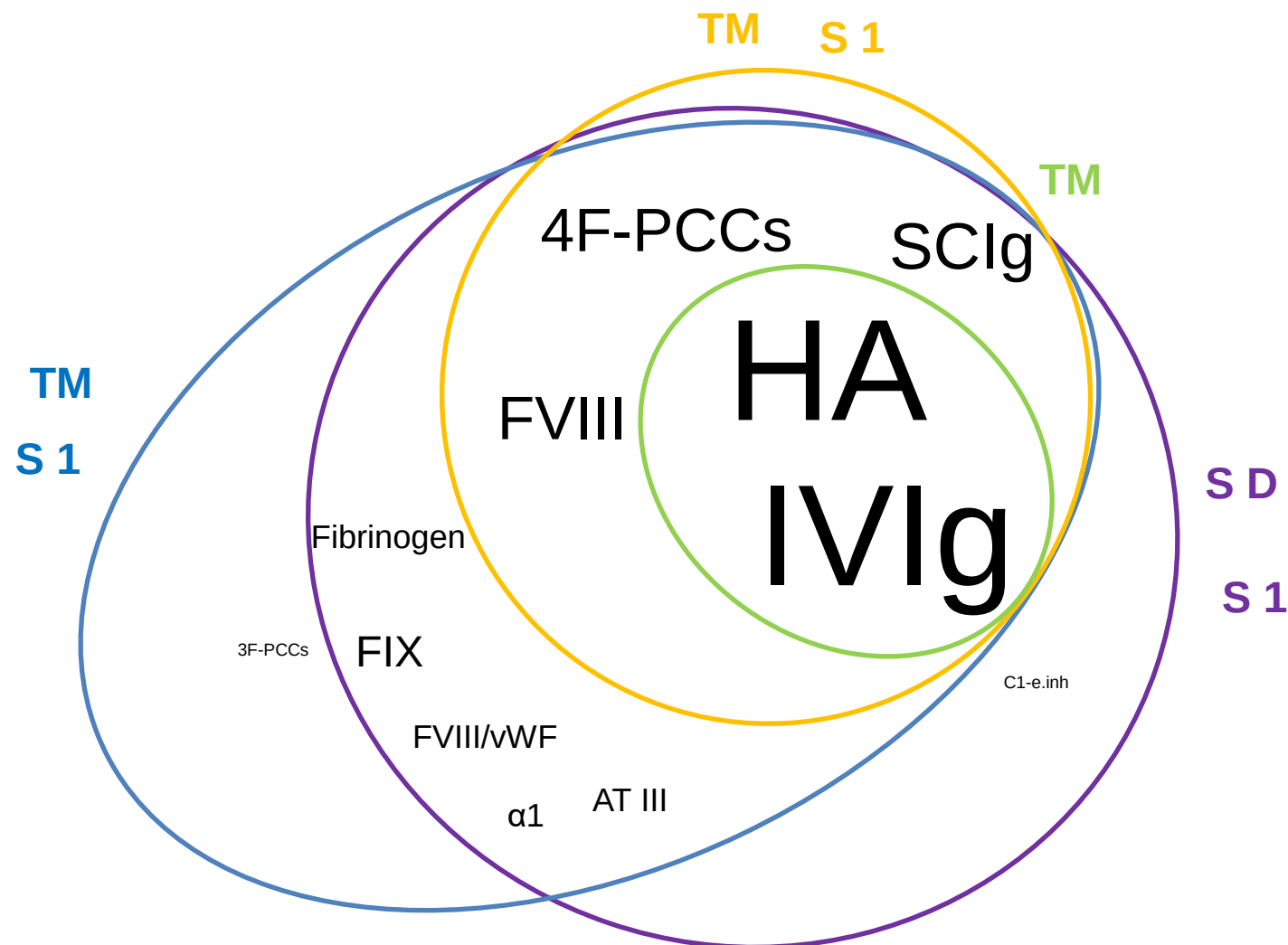
### Q10 - PDMPs returned - Total active ingredients returned to EU MS according to the manufacturing model.

|       | Manufacturing Models | Albumin | IVIg | SCIg | FVIII | FVIII/VWF | FIX | 3F-PPCs | 4F-PPCs | Fibrinogen | Alpha-1-antitrypsin | Antithrombin | C1-esterase inhibitor | Total active ingredients returned |
|-------|----------------------|---------|------|------|-------|-----------|-----|---------|---------|------------|---------------------|--------------|-----------------------|-----------------------------------|
| MS 17 | TM                   |         |      |      |       |           |     |         |         |            |                     |              |                       | 3                                 |
| MS 11 | TM                   |         |      |      |       |           |     |         |         |            |                     |              |                       | 11                                |
| MS 15 | TM                   |         |      |      |       |           |     |         |         |            |                     |              |                       | 2                                 |
| MS 23 | S                    |         |      |      |       |           |     |         |         |            |                     |              |                       | 3                                 |
| MS 3  | TM                   |         |      |      |       |           |     |         |         |            |                     |              |                       | 7                                 |
| MS 19 | TM                   |         |      |      |       |           |     |         |         |            |                     |              |                       | 5                                 |
| MS 20 | TM                   |         |      |      |       |           |     |         |         |            |                     |              |                       | 3                                 |
| MS 6  | S                    |         |      |      |       |           |     |         |         |            |                     |              |                       | 4                                 |
| MS 4  | S                    |         |      |      |       |           |     |         |         |            |                     |              |                       | 11                                |
| MS 9  | S                    |         |      |      |       |           |     |         |         |            |                     |              |                       | 11                                |
| MS 12 | TM                   |         |      |      |       |           |     |         |         |            |                     |              |                       | 2                                 |
| MS 21 | TM                   |         |      |      |       |           |     |         |         |            |                     |              |                       | 6                                 |
| MS 5  | TM                   |         |      |      |       |           |     |         |         |            |                     |              |                       | 3                                 |

## Section B. Information on plasma fractionated into PDMPs

### Q10 - PDMPs returned

13/22 Answers



- All PDMPs return
- Drivers + 1 PDMP
- Only drivers
- No PDMPs return (free market purchasing)

**Legend**  
**TM:** toll-manufacturing agreements  
**S D:** sale to different companies  
**S 1:** sale to one company on exclusive basis

## PRODOTTI RESTITUITI IN CONTO-LAVORO – ANNO 2022

| REGIONI | Albumina   | FVIII      | FVIII/vWF | FIX       | COMPLESSO<br>PROTR.3 FATTORI | IVIg      | IGSc    |
|---------|------------|------------|-----------|-----------|------------------------------|-----------|---------|
|         | g          | UI         | UI        | UI        | UI                           | g         | g       |
| NAIP    | 6.136.040  | 8.205.000  | 5.580.000 | -         | 2.872.500                    | 1.073.245 | 59.500  |
| RIPP    | 6.230.570  | 9.198.000  | 180.000   | 595.000   | 8.719.500                    | 950.890   | 22.380  |
| Pla.Net | 4.070.350  | 11.192.000 | 1.486.000 | 3.098.000 | 7.253.200                    | 795.090   | 84.026  |
| LPS     | 6.492.070  | 15.414.000 | -         | 1.451.000 | 10.142.500                   | 949.055   | 4.672   |
| ITALIA  | 22.929.030 | 44.009.000 | 7.246.000 | 5.144.000 | 28.987.700                   | 3.768.280 | 170.578 |

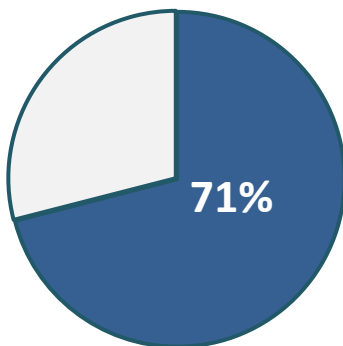
| REGIONI | AT         | Fibrinogeno | Plasma S/D | PROTEINA C | CCPa    | CCP4F | ALFA-1 |
|---------|------------|-------------|------------|------------|---------|-------|--------|
|         | UI         | g           | mL         | UI         | UF      | UI    | g      |
| NAIP    | 10.282.000 | 9.480       | 886.200    | -          | -       | -     | -      |
| RIPP    | 38.220.000 | -           | 1.131.400  | -          | -       | -     | 3.692  |
| Pla.Net | 25.408.000 | -           | 8.708.400  | 275.000    | 686.000 | -     | -      |
| LPS     | 18.443.000 | -           | 4.618.000  | -          | -       | -     | -      |
| ITALIA  | 92.353.000 | 9.480       | 15.344.000 | 275.000    | 686.000 | -     | 3.692  |

Valorizzazione economica a C.M.U. 2022 =

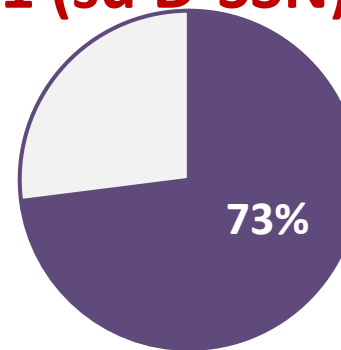
**€ 335.541.000**

## AUTOSUFFICIENZA MPD – ITALIA – ANNO 2021 (su D-SSN)

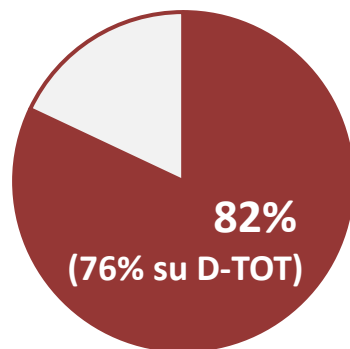
ALBUMINA



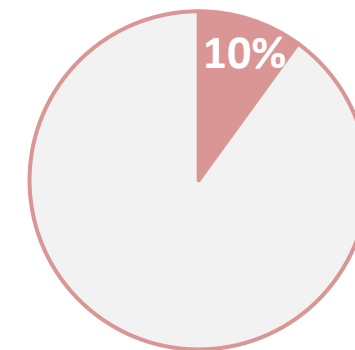
ANTITROMBINA



IV IMMUNOGLOBULINE\*\*

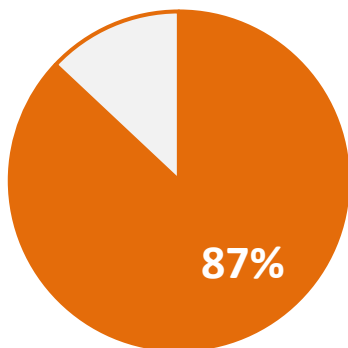


SC IMMUNOGLOBULINE

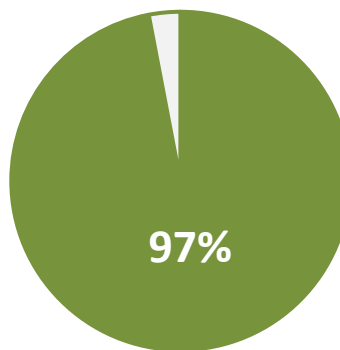


FIX+CCP3

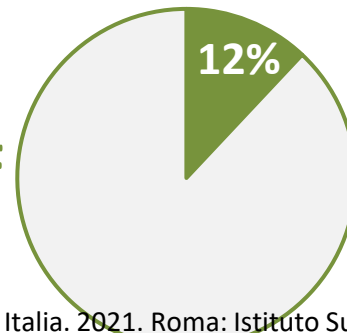
(solo CCP3  
autosufficienza=91%  
Solo FIX  
autosufficienza=63%)



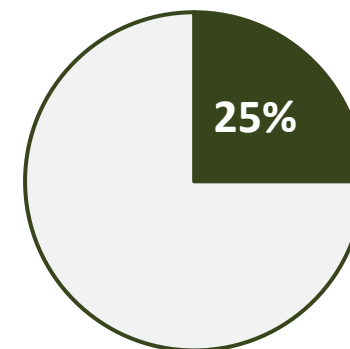
FVIII\*



FVIII/vWF



FIBRINOGENO °



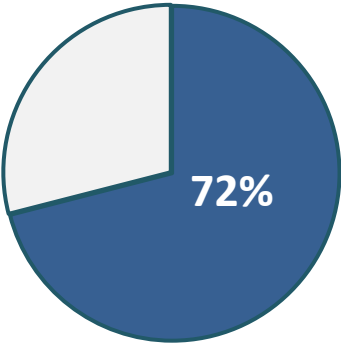
\*100% of total demand for contract-manufactured products

\*\* The value not includes Pentaglobin™

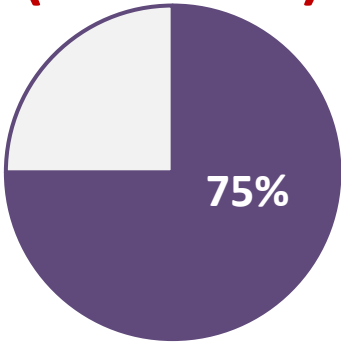
° on the total demand for contract-manufactured products

# AUTOSUFFICIENZA MPD – ITALIA – ANNO 2022 (su D-SSN)

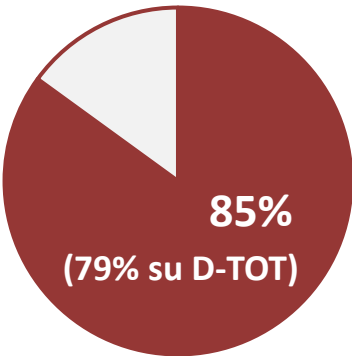
ALBUMINA



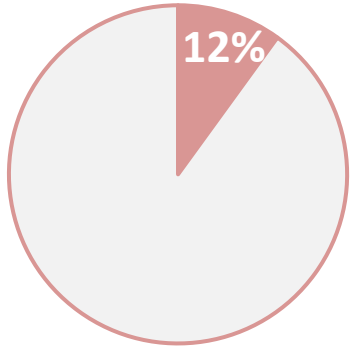
ANTITROMBINA



IV IMMUNOGLOBULINE\*\*

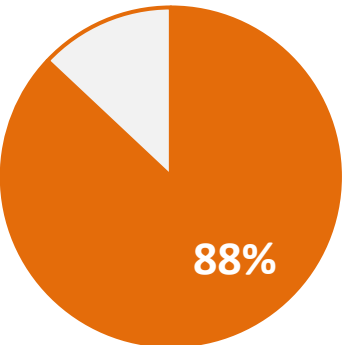


SC IMMUNOGLOBULINE

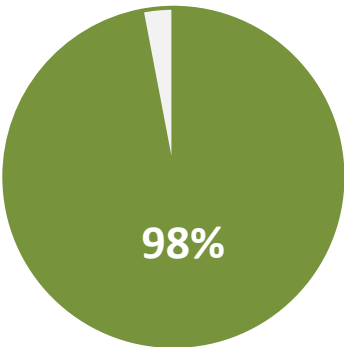


FIX+CCP3

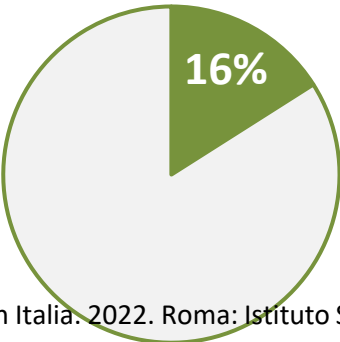
(solo CCP3  
autosufficienza=91%  
Solo FIX  
autosufficienza=75%)



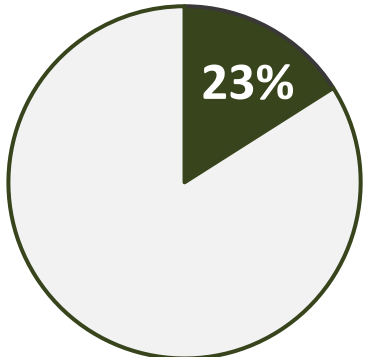
FVIII\*



FVIII/vWF



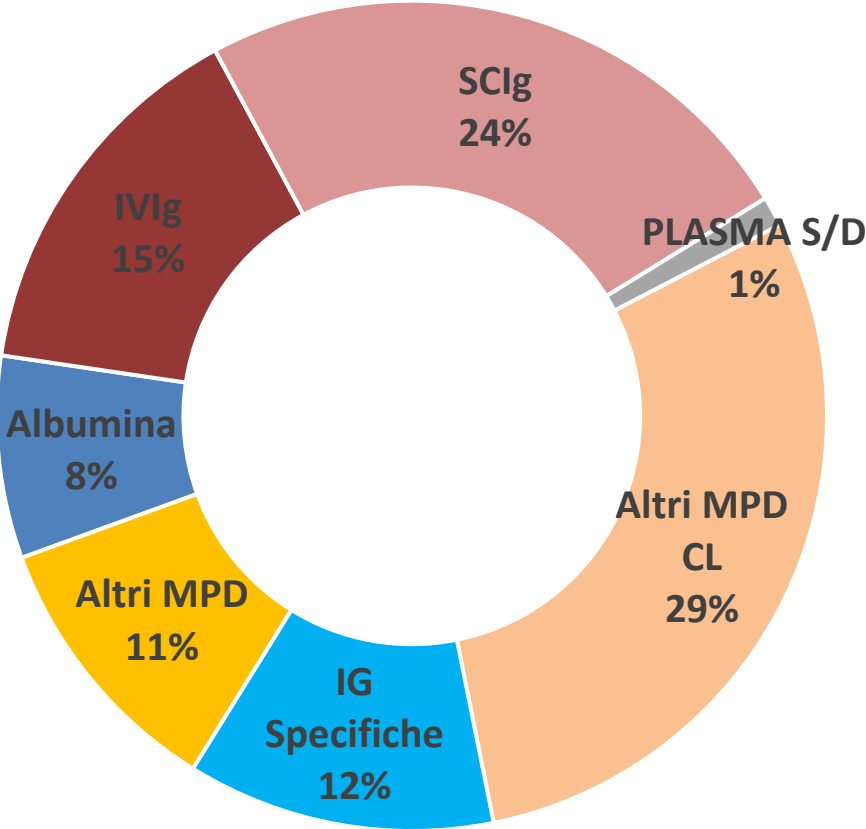
FIBRINOGENO °



\*100% of total demand for contract-manufactured products  
\*\* The value not includes Pentaglobin™

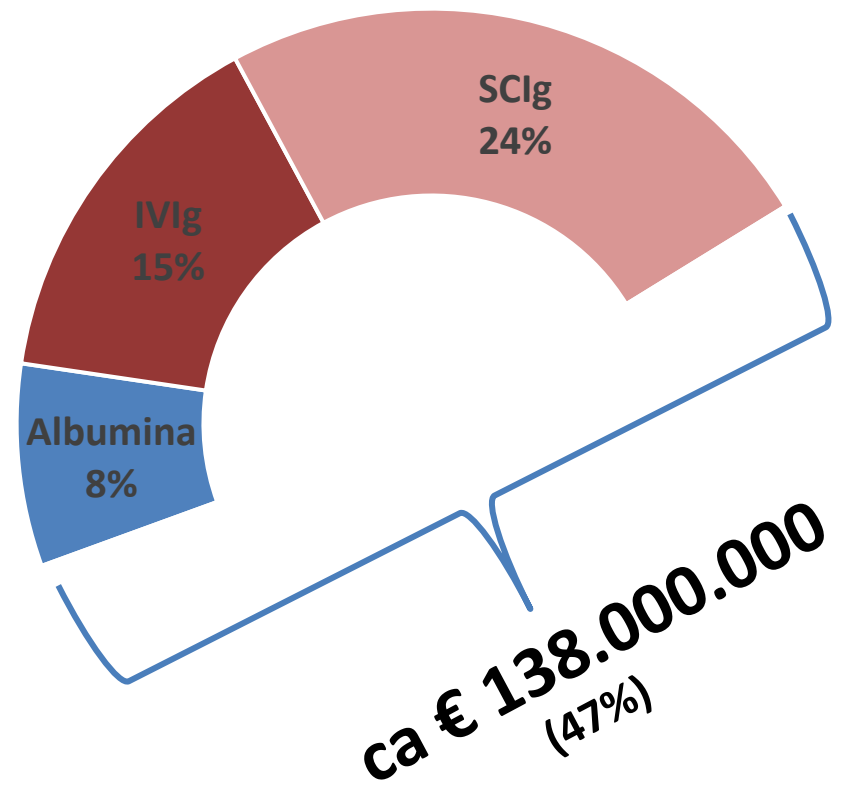
° on the total demand for contract-manufactured products

STIMA DELLA SPESA PER L'ACQUISTO DI MPD - ANNO 2022



| Tipo MPD      | Stima spesa (euro) |
|---------------|--------------------|
| Albumina      | 23.303.289         |
| IVIg          | 43.758.939         |
| SCIg          | 71.140.748         |
| PLASMA S/D    | 3.434.683          |
| Altri MPD CL  | 87.039.706         |
| IG Specifiche | 35.458.173         |
| Altri MPD     | 31.336.029         |
| TOTALE SPESA  | 295.471.567        |

# STIMA DELLA SPESA PER L'ACQUISTO DI MPD - ANNO 2022



| Tipo MPD      | Stima spesa (euro) |
|---------------|--------------------|
| Albumina      | 23.303.289         |
| IVIg          | 43.758.939         |
| SCIg          | 71.140.748         |
| PLASMA S/D    | 3.434.683          |
| Altri MPD CL  | 87.039.706         |
| IG Specifiche | 35.458.173         |
| Altri MPD     | 31.336.029         |
| TOTALE SPESA  | 295.471.567        |

# Monitoring the demand for PDMPs

## Section B. Information on plasma fractionated into PDMPs

### Q10 - PDMPs returned - Total active ingredients returned to EU MS according to the manufacturing model.

|       | Manufacturing Models | Albumin | IVIg | SCIg | FVIII | FVIII/vWF | FIX | 3F-PPCs | 4F-PPCs | Fibrinogen | Alpha-1-antitrypsin | Antithrombin | C1-esterase inhibitor | Total active ingredients returned |
|-------|----------------------|---------|------|------|-------|-----------|-----|---------|---------|------------|---------------------|--------------|-----------------------|-----------------------------------|
| MS 17 | TM                   |         |      |      |       |           |     |         |         |            |                     |              |                       | 3                                 |
| MS 11 | TM                   |         |      |      |       |           |     |         |         |            |                     |              |                       | 11                                |
| MS 15 | TM                   |         |      |      |       |           |     |         |         |            |                     |              |                       | 2                                 |
| MS 23 | S                    |         |      |      |       |           |     |         |         |            |                     |              |                       | 3                                 |
| MS 3  | TM                   |         |      |      |       |           |     |         |         |            |                     |              |                       | 7                                 |
| MS 19 | TM                   |         |      |      |       |           |     |         |         |            |                     |              |                       | 5                                 |
| MS 20 | TM                   |         |      |      |       |           |     |         |         |            |                     |              |                       | 3                                 |
| MS 6  | S                    |         |      |      |       |           |     |         |         |            |                     |              |                       | 4                                 |
| MS 4  | S                    |         |      |      |       |           |     |         |         |            |                     |              |                       | 11                                |
| MS 9  | S                    |         |      |      |       |           |     |         |         |            |                     |              |                       | 11                                |
| MS 12 | TM                   |         |      |      |       |           |     |         |         |            |                     |              |                       | 2                                 |
| MS 21 | TM                   |         |      |      |       |           |     |         |         |            |                     |              |                       | 6                                 |
| MS 5  | TM                   |         |      |      |       |           |     |         |         |            |                     |              |                       | 3                                 |



<https://www.centronazionalesangue.it/rapporti-tecnici/>

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Domenico Di Giorgio – AIFA  
Isabella Marta - AIFA  
Sandra Salinetti – PS, ISS  
Giuseppe Traversa - AIFA

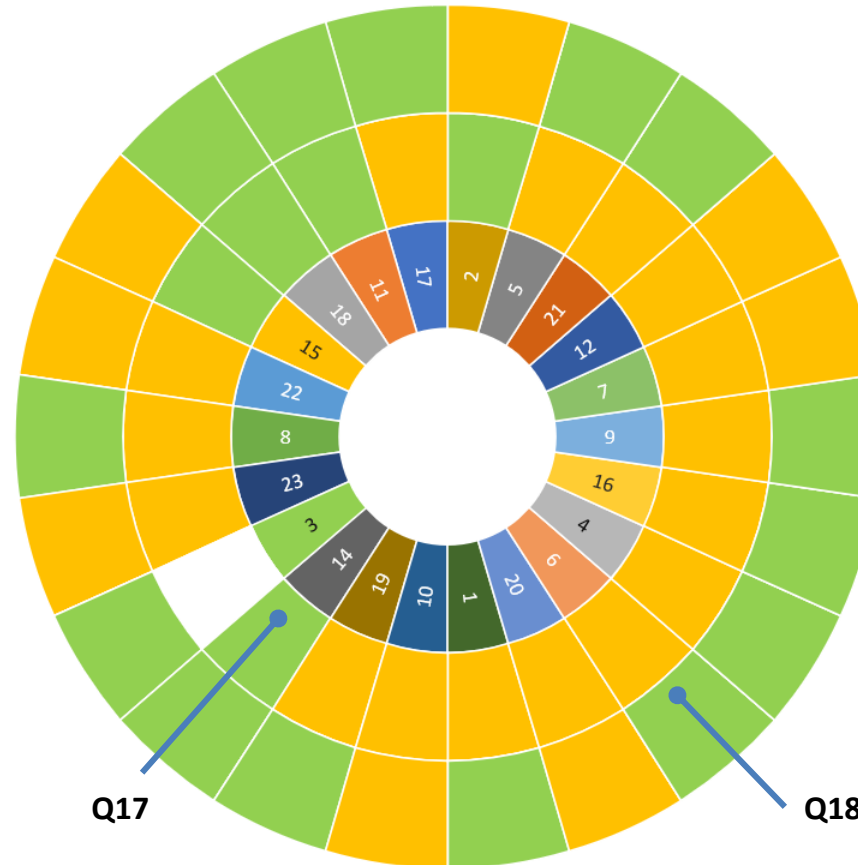
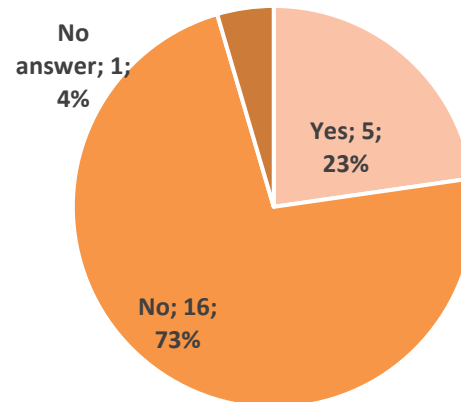
# SELF-ADVERTISING

# Appropriateness of the demand for PDMPs

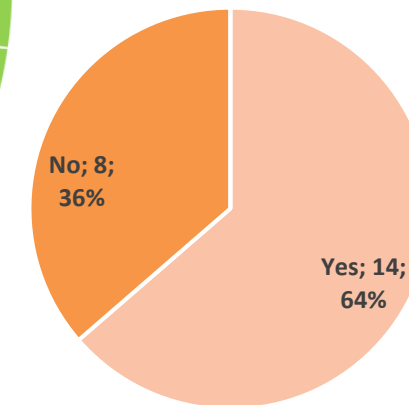
## Section C. Information on legislative framework/programme/policy on collection and prioritising use

### Q17 - Q18 Appropriate and rational use of PDMPs

Q17: Does your Country have a specific **legislative framework** on the **appropriate and rational use** of PDMPs?



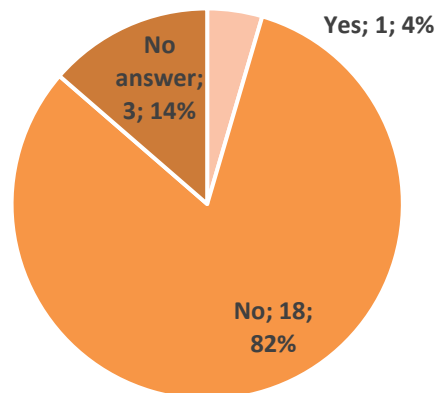
Q18: Does your Country have a **specific programme/policy** (e.g. guidance documents, recommendations) on the **appropriate and rational clinical use** of PDMPs?



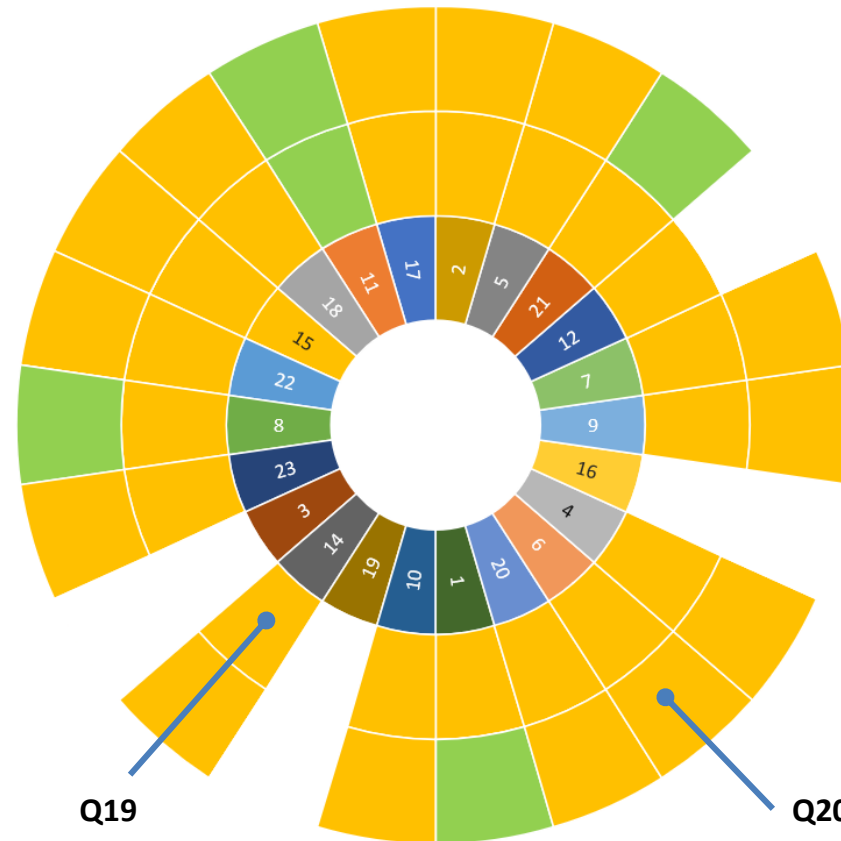
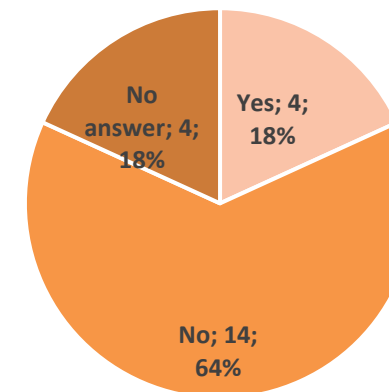
## Section C. Information on legislative framework/programme/policy on collection and prioritising use

### Q19 - Q20 Prioritising the use of PDMPs

Q19: Does your Country have a specific **legislative framework** on prioritising use of PDMPs?



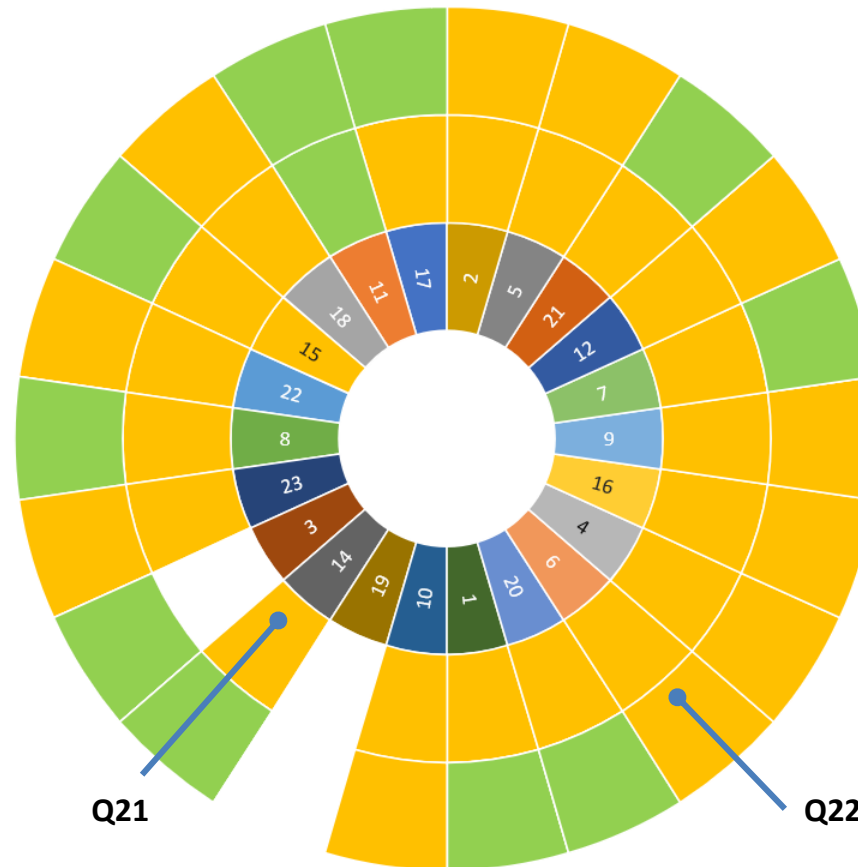
Q20: Are there any **guidelines/indications** on prioritising use of PDMPs?



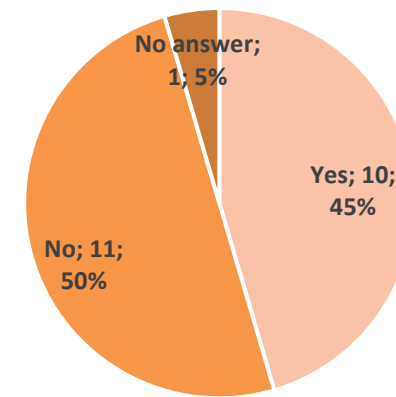
## Section C. Information on legislative framework/programme/policy on collection and prioritising use

Q21 - Q22

and shortages of PDMPs



Q22: Does your Country have a **specific legislative framework/policy** on PDMPs **shortage** (e.g. mandatory storage and/or contingency rules)?



# CNS - AIFA Guidelines



## INVENTORY PHASE ACTIVITY AND ALLOCATION CRITERIA ACCORDING IMMUNOGLOBULINS AVAILABILITY

The following table shows the IG management criteria based on the availability of IGs.

Table 2. Inventory phase activity and IGs allocation criteria (adapted from: Canadian Blood Committee on Blood and Blood Products. The National Plan of Management of Shortages of Immunoglobulin Products – Interim Guidance, 2020-07-27).

| Inventory level      | Description and activities                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |
|----------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Green                | <ul style="list-style-type: none"><li>IG supply/inventory meets demand.</li><li>Follow jurisdictional best practice recommendations for use (guides, modality of administration, and doses).</li><li>Use the lowest IG dose for the shortest duration required to achieve the desired clinical outcome.</li><li>For ongoing therapy, ensure the achievement of measurable benefit in patients with no demonstrable benefit.</li><li>Prior to starting IG treatment, consider use of all other safe, effective therapies.</li><li>Where use is indicated, confirm that use aligns with the patient's best interests.</li><li>Use a dose calculator based on adjusted body weight, and appropriate to the patient's clinical condition.</li></ul>                                                                                                                                                                                                                                                                                                      |
| Green Advisory Phase | <ul style="list-style-type: none"><li>IG supply/inventory levels are reduced or there are signs that short-term IG supply will be reduced.</li><li>Reduce use by 10 to 20%:</li><li>Continue to follow all the actions outlined in Green phase.</li><li>Round down IG treatment doses and frequency. Re-assess treatment to find the minimal effective dose and optimize IG use.</li><li>Review stocking practices and maintain the minimum inventory.</li><li>Reduce the refill volume for patients on home infusion products.</li><li>Consider the use of alternative therapies.</li><li>Initiate actions to prepare for the potential escalation to Amber or Red (in the event of an SCIG shortage), or other options:</li><li>Identifying patients that can be switched to SCIG (or IVIG) in the event of an SCIG shortage, or other options.</li><li>Initiating local and provincial processes to support the use of a red phase advisory.</li></ul>                                                                                            |
| Amber                | <ul style="list-style-type: none"><li>IG supply/inventory levels are low for a short or prolonged period. Red phase actions should be initiated.</li><li>Continue to follow all the actions outlined in Green phase and Green Advisory Phase.</li><li>Use the lowest IG dose for the shortest duration required to achieve the desired clinical outcome.</li><li>Implement screening of all IG orders within the hospital system.</li><li>There is a critical and prolonged IG shortage. Reduce use by over 50%:</li><li>Limit IG use to clinical circumstances when there are:</li><li>No viable alternatives; and/or</li><li>The condition is life-threatening or there is a high risk of severe morbidity or mortality.</li><li>Identified in the table below.</li><li>Have each case and dose approved by a formally established peer committee as per local jurisdictional guidance.</li><li>File a written copy of the decision in the patient's medical record and send another copy to Transfusion Medicine Services (blood bank).</li></ul> |
| Red                  | <ul style="list-style-type: none"><li>There is a critical and prolonged IG shortage. Reduce use by over 50%:</li><li>Limit IG use to clinical circumstances when there are:</li><li>No viable alternatives; and/or</li><li>The condition is life-threatening or there is a high risk of severe morbidity or mortality.</li><li>Identified in the table below.</li><li>Have each case and dose approved by a formally established peer committee as per local jurisdictional guidance.</li><li>File a written copy of the decision in the patient's medical record and send another copy to Transfusion Medicine Services (blood bank).</li></ul>                                                                                                                                                                                                                                                                                                                                                                                                     |

It is essential that, in conditions of important and critical shortage, serious pathological conditions will be prioritised when no therapeutic alternatives are available. In Italy, the latest recommendations of the Italian Society of Transfusion Medicine and Immunohaematology (SIMITI) on the correct use of blood components and PDMPs date back to 2008; in particular, a list of clinical conditions in which the routine use of IVIG is not recommended and a list of inappropriate indications for the use of IVIGs are included.

## CRITERIA FOR RECOGNISED IMMUNE

The main criteria for ensuring an appropriate use of IVIGs, divided by therapeutic area and National Advisory Committee on Shortages of Immunoglobulin Products.

The list of conditions and guidance is circumstances in which a condition is life-threatening or there are not enough IGs available during the development of the IGs Shortage.

## LEGEND

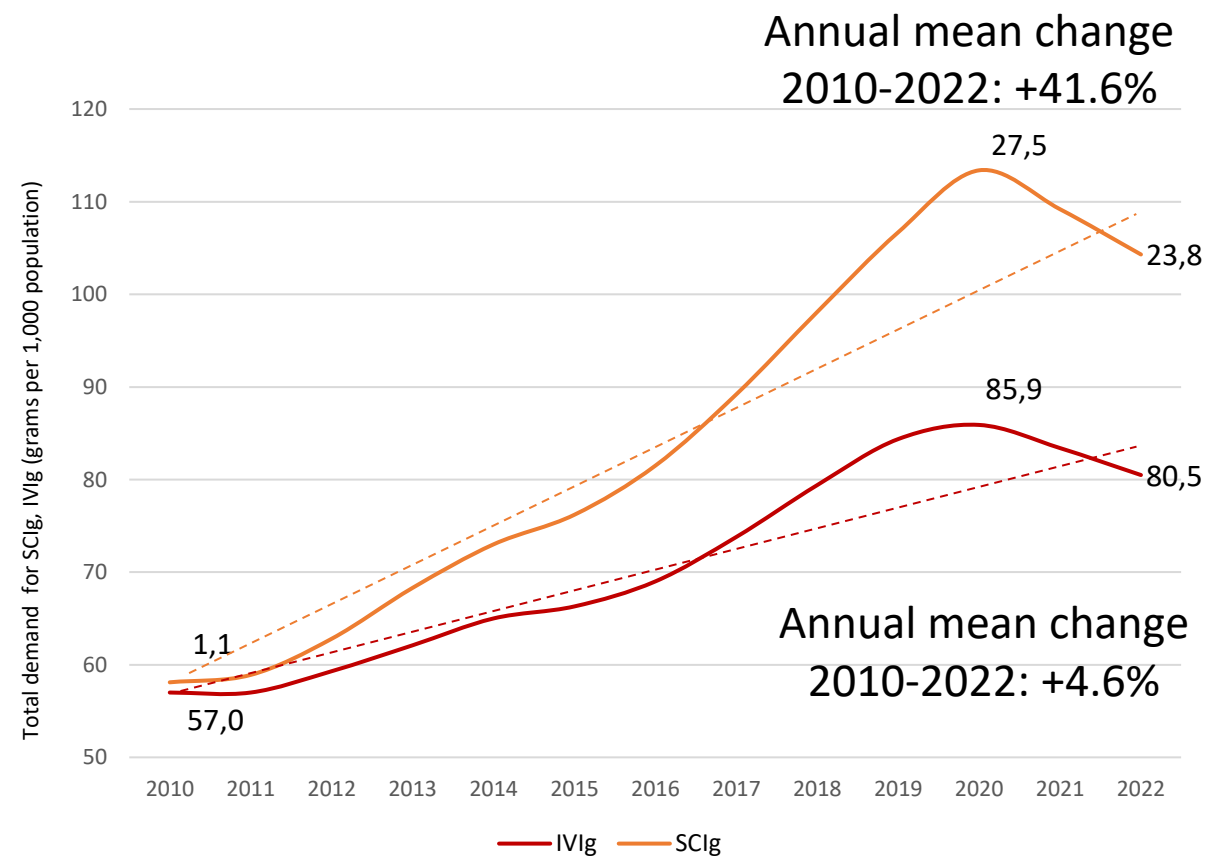
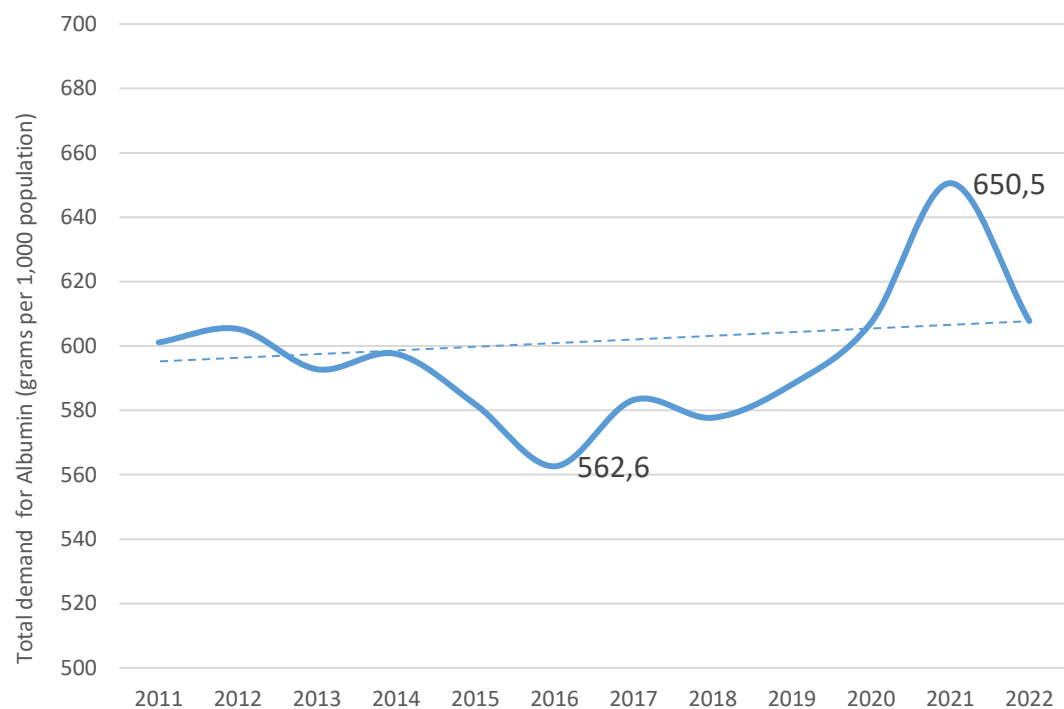
|  |                                                                                                            |
|--|------------------------------------------------------------------------------------------------------------|
|  | IG supply/inventory levels are low for a short or prolonged period. Red phase actions should be initiated. |
|  | There is a critical and prolonged IG shortage. Reduce use by over 50%:                                     |
|  | IG supply/inventory levels are low for a short or prolonged period. Red phase actions should be initiated. |

## E) NEUROLOGY

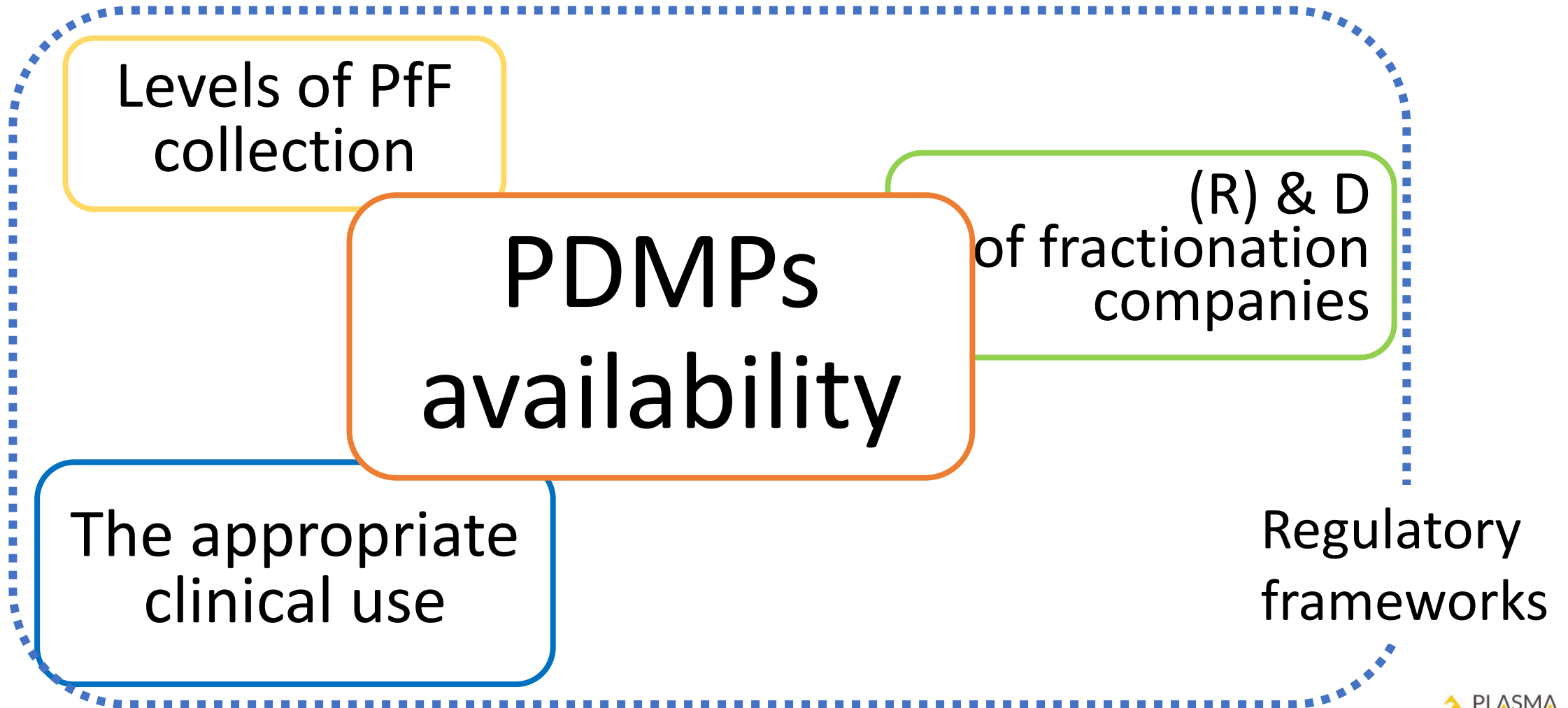
| CONDITION                                                                  | CRITERIA FOR ENSURING APPROPRIATE AND PRIORITY USE OF IGs IN CONDITIONS OF SHORTAGES                                                                                                                                                                                                                                                                                                                                               |
|----------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Acute disseminated encephalomyelitis (ADEM)                                | <ul style="list-style-type: none"><li>In cases of severe disease and failure, contraindication or intolerance to other therapeutic options<sup>1</sup>.</li></ul>                                                                                                                                                                                                                                                                  |
| Autoimmune Encephalitis                                                    | <ul style="list-style-type: none"><li>In cases of severe disease and failure, contraindication or intolerance to other therapeutic options<sup>1</sup>.</li></ul>                                                                                                                                                                                                                                                                  |
| Chronic inflammatory demyelinating polyneuropathy (CIDP) <sup>2</sup>      | <ul style="list-style-type: none"><li>Consider steroids and/or plasma exchange whenever possible.</li><li>Initial and maintenance treatment in cases of failure, contraindication or intolerance to other forms of immunosuppressive therapy<sup>1</sup>.</li></ul>                                                                                                                                                                |
| Graves' ophthalmopathy                                                     | <ul style="list-style-type: none"><li>In cases of vision-threatening severe disease with failure, contraindications or intolerance to other therapeutic options.</li></ul>                                                                                                                                                                                                                                                         |
| Guillain-Barré syndrome (GBS) or variants including Miller Fisher syndrome | <ul style="list-style-type: none"><li>Preferential use for initial treatment of GBS if plasma exchange not available or feasible.</li><li>A second course of IVIG may be considered in patients with clearly documented secondary deterioration, only after consulting a specialist.</li><li>In cases of failure, contraindication or intolerance to plasma exchange OR in cases where plasma exchange is not available.</li></ul> |
| Lambert-Eaton myasthenic syndrome (LEMS)                                   | <ul style="list-style-type: none"><li>In cases of severe disease and failure, contraindication or intolerance to other therapeutic options<sup>1</sup>.</li></ul>                                                                                                                                                                                                                                                                  |
| Multifocal motor neuropathy (MMN) <sup>2</sup>                             | <ul style="list-style-type: none"><li>For front-line therapy<sup>1</sup>.</li></ul>                                                                                                                                                                                                                                                                                                                                                |
| Myasthenia gravis (MG)                                                     | <ul style="list-style-type: none"><li>In cases of severe exacerbation, myasthenic crisis or in preparation for urgent or semi-urgent surgery.</li><li>In cases of severe exacerbation, myasthenic crisis or in preparation for urgent or semi-urgent surgery with failure, contraindication, intolerance or lack of</li></ul>                                                                                                      |

<https://www.centronazionalesangue.it/linee-guida/>

# Demand for drivers 2010 - 2022



# (main) factors influencing the availability of PDMPs



# Collection? To what extent?

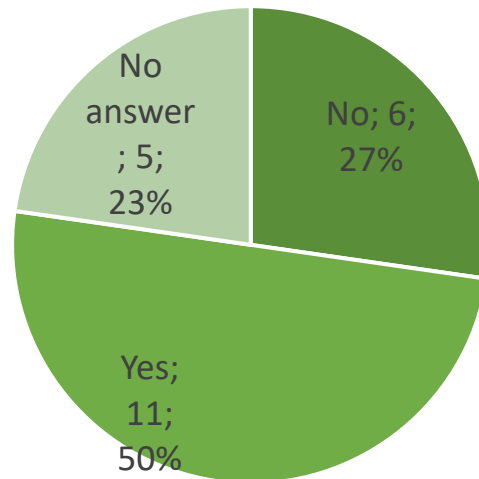


Maintain  
the economic attractiveness of  
national and European markets  
in a global setting,  
avoiding any kind of  
competition based on  
national (self-referring) price  
policies among MS

## Section E. Financial aspects

**Q39 - In the last years 2019-2022, has there been an increase in the price for immunoglobulins in your Country?**

**17 answer**  
**5 no answer**



**Q40 - Can you describe the changes in Immunoglobulin prices observed during these years?**

**2019: 5 answer**  
**2020: 3 answer**  
**2021: 3 answer**  
**2022: 5 answer**

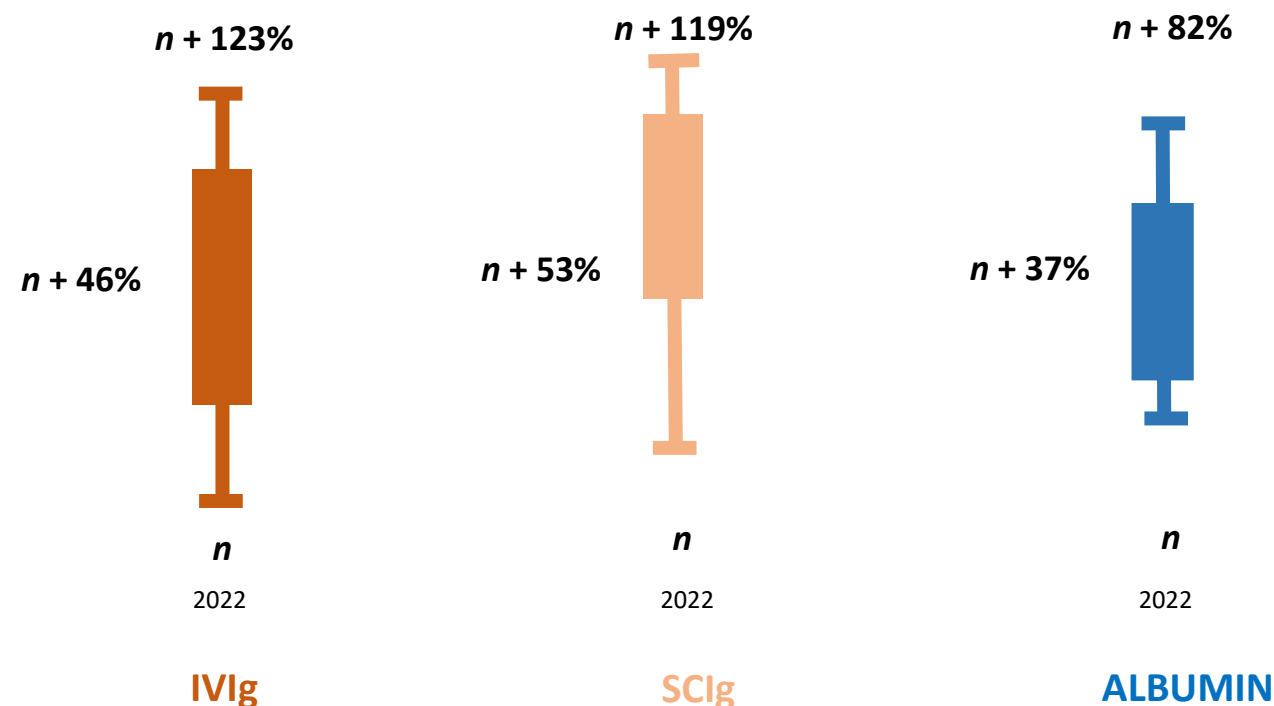


**Δ 2022 vs2019**

|            |             |
|------------|-------------|
| <b>MS1</b> | <b>+49%</b> |
| <b>MS2</b> | <b>+23%</b> |
| <b>MS3</b> | <b>+55%</b> |
| <b>MS4</b> | <b>+24%</b> |
| <b>MS5</b> | <b>+7%</b>  |

## Section E. Financial aspects

**Q35 – If the market prices (final price by end user, preferably excluding VAT and local fees) are publicly known, what is the market mean price observed in the past years?**



# How to avoid?

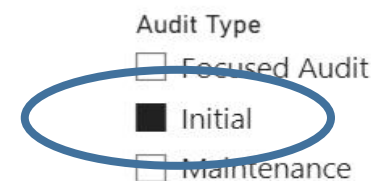
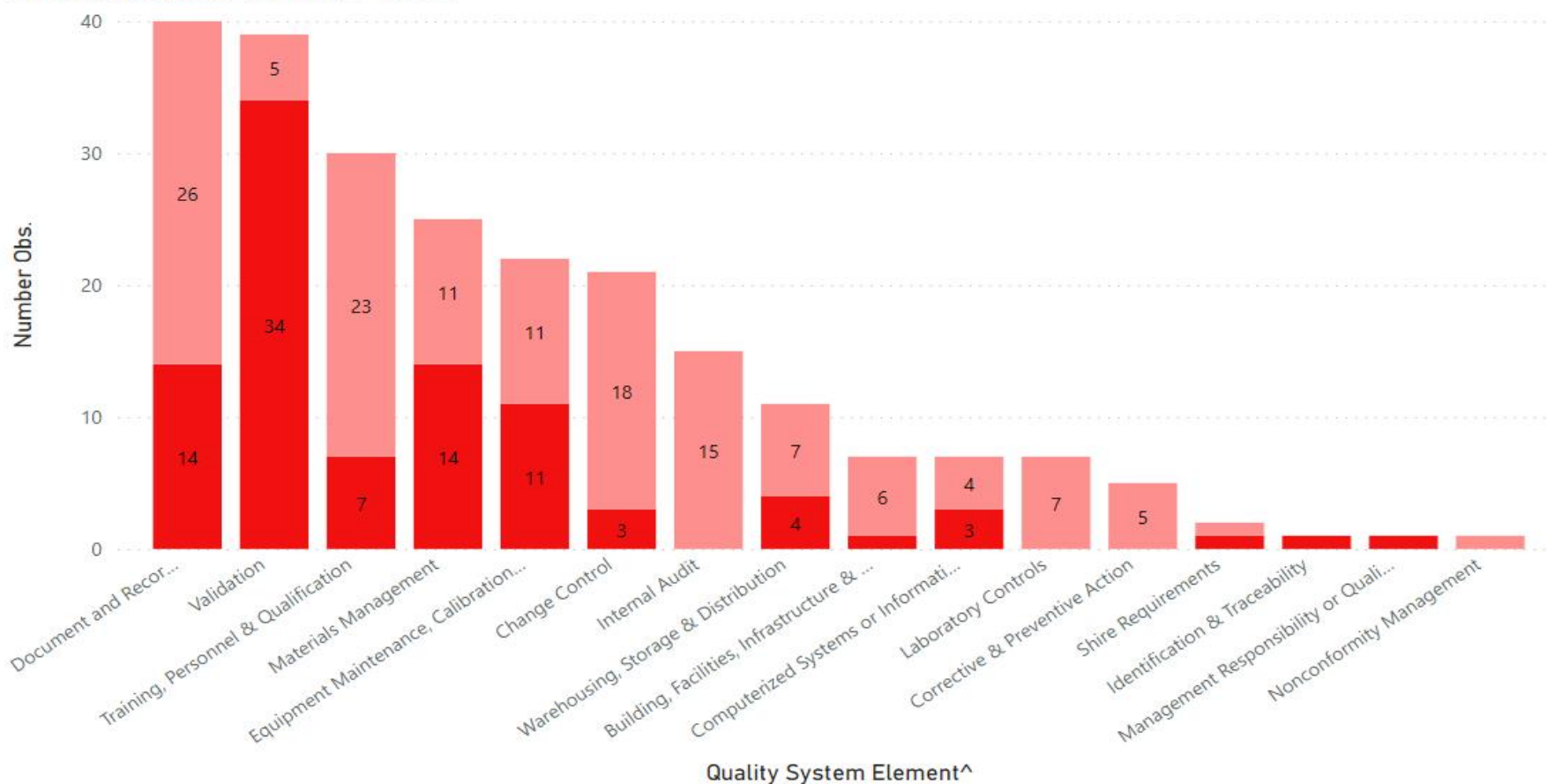
## Operational cooperation with fractionation companies

- Trasparency and sharing with all operating companies in the MS on the needs (out of the fractionation of domestic plasma) in order to enable the fractionators an appropriate planning of collection, manufacturing, and best allocation of PDMPs
- Common approach to the «growth» of QMS in BEs

# Observations per Region in Italy

## Observation per QSE

Observation Classification ● Major ● Minor



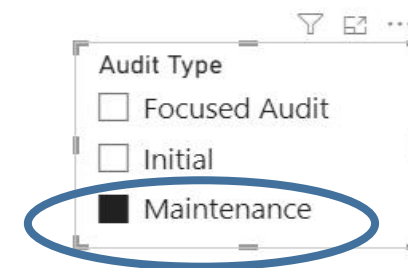
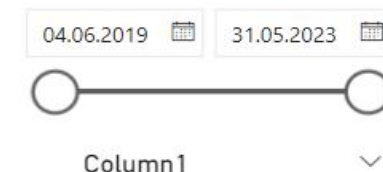
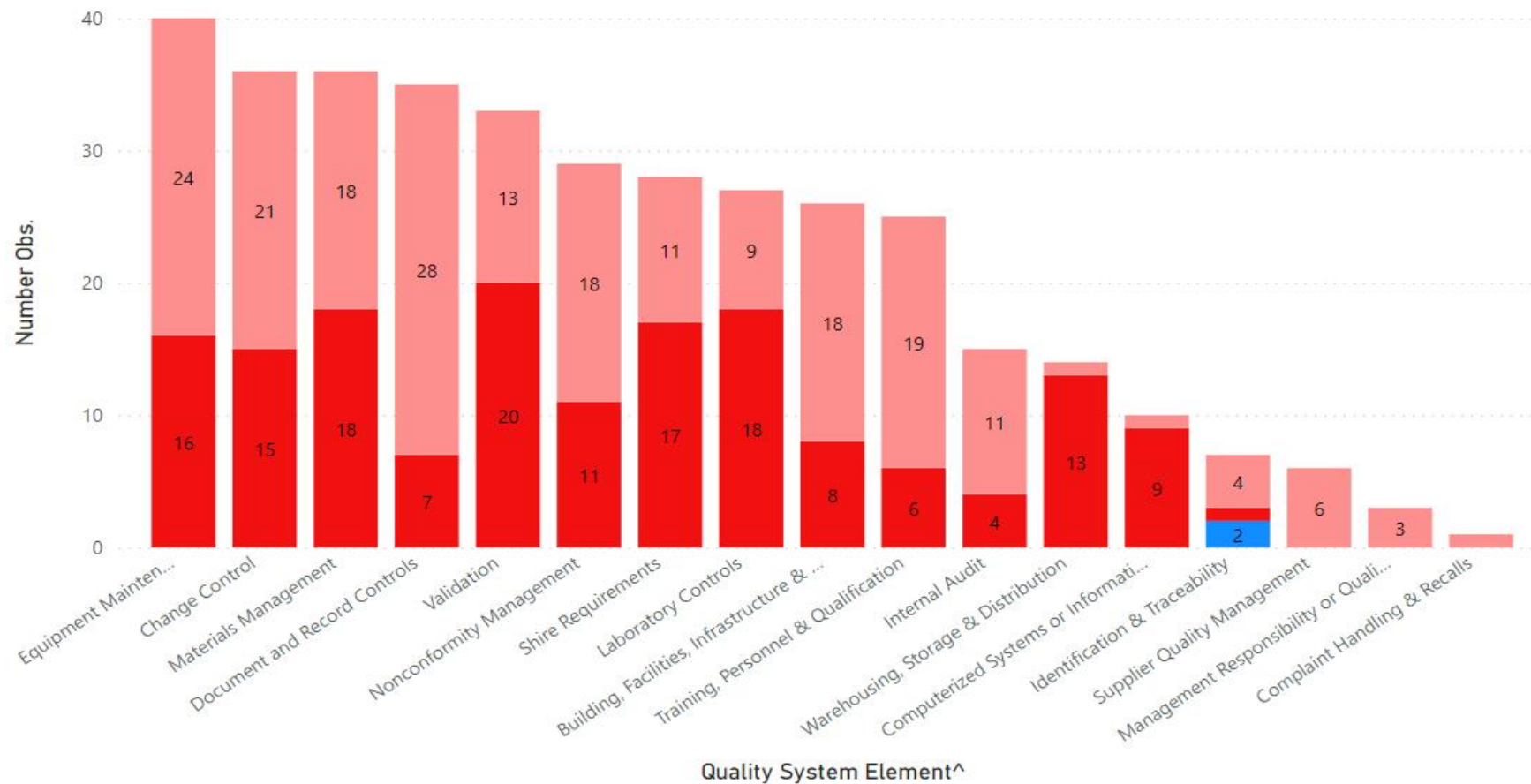
NUM. AUDITS

72

# Observations per Region in Italy

## Observation per QSE

Observation Classification ● Critical ● Major ● Minor



NUM. AUDITS

69

# Collection? To what extent?

The SUPPLY project aims to increase and strengthen the resilience of plasma collection within the public sector in the European Union (EU) to enable a stable, appropriate, and sufficient supply of Plasma-derived medicinal products (PDMPs) for patients both in a general situation as well as in times of crises

In Italy, signals of a real consciousness of PDMPs-related issues started to give some positive results in term of growth of collection and appropriate utilisation.

What if, this will be observed in all EU MS including European countries that at the moment are not manufacturing PDMPs from domestic plasma?

**It doesn't happen... (pessimism of the intellect)**

**...but if it will happen... (optimism of the will)**

Will the fractionators have the production capacity to fulfill the needs coming from «the market of fractionation of domestic plasma»?

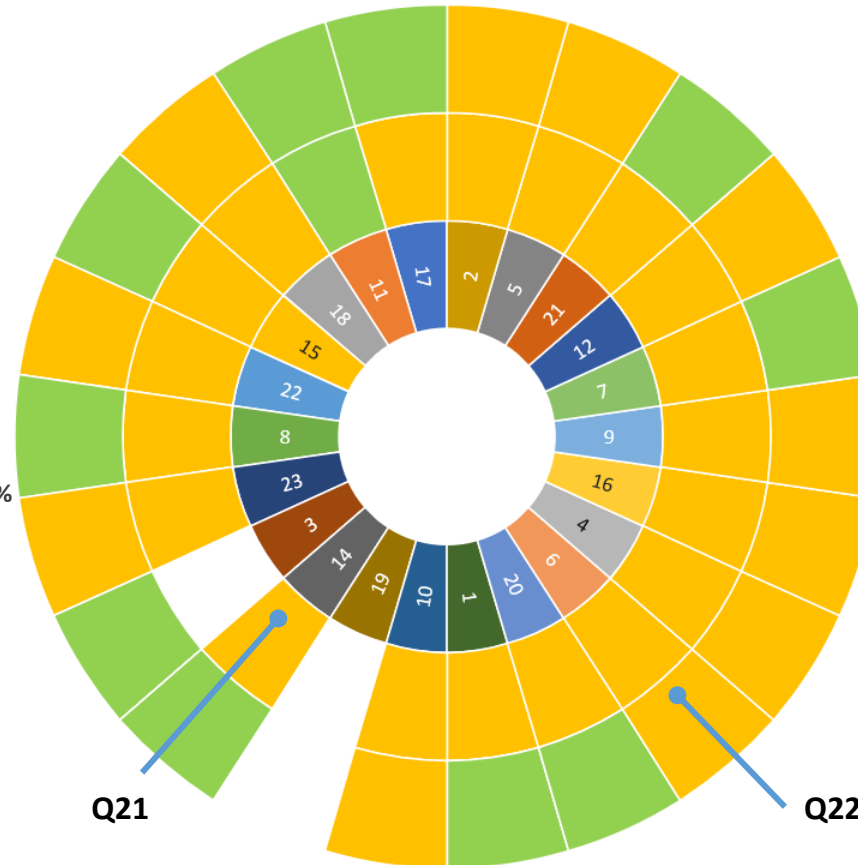
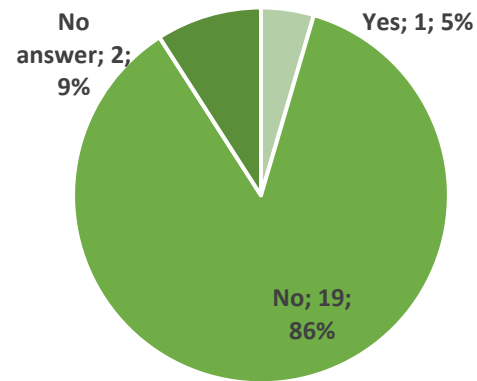
What will be the role of EU funding agencies in supporting the collection and the growth of the production capacity of the fractionation industry?

**...at last**

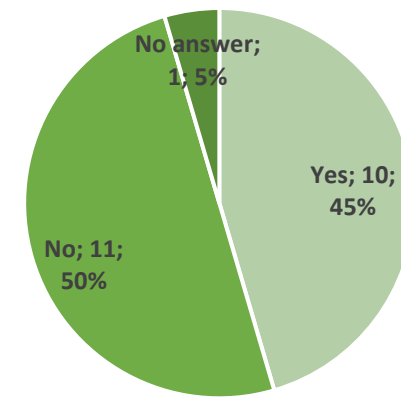
## Section C. Information on legislative framework/programme/policy on collection and prioritising use

### Q21 - Q22 Excesses and shortages of PDMPs

Q21: Does your Country have a **specific legislative framework/policy on exceeding** PDMPs?



Q22: Does your Country have a **specific legislative framework/policy on PDMPs shortage** (e.g. mandatory storage and/or contingency rules)?



## Humanitarian shipment from Italy to provide patients in Gaza with plasma-derived medicinal products

The first shipment, scheduled this week in January, includes **500,000 IUs of coagulation Factor VIII** concentrates.

These are **life-saving** medicines for **patients with haemophilia** who due to the ongoing conflict no longer have access to treatments.



## Humanitarian shipment from Italy to provide patients in Gaza with plasma-derived medicinal products

The PDMPs, **exceeding Italian national needs**, come from **voluntary, non-remunerated donations**, on this occasion, from donors in Emilia-Romagna Region.

The shipment to the Gaza Strip is handled by the **EU Humanitarian Air Bridge**, within the **European Civil Protection and Humanitarian Aid Operations (ECHO)**.

The **Egyptian and Palestinian Red Crescent Societies** are providing internal transfer and distribution.





**CENTRO  
NAZIONALE  
SANGUE**

# THE SUPPLY OF PLASMA-DERIVED MEDICINAL PRODUCTS IN THE FUTURE OF EUROPE

**23-24 APRIL 2024**

*See you in Roma!*

# PEACE

(again and again),

# Please

THE SUPPLY OF PLASMA-DERIVED MEDICINAL PRODUCTS IN THE  
FUTURE OF EUROPE

23-24 APRIL 2024

*See you in Roma!*