C/o European Blood Alliance (Project Lead)
Clos Chapelle-aux-Champs 30 bte 1.30.30
B-1200 Brussels
Belgium

info@supply-project.eu
www.supply-project.eu

WP: 1 Document type: Report Version: 1

Deliverable Report D1.1

D1.1 Scenario Evaluation Plan

Co-funded by the European Union

This report is part of the project "101056988/SUPPLY" which has received funding from the European Union's EU4Health Programme (2021-2027). The content of this report represents the views of the author only and is his/her sole responsibility; it can not be considered to reflect the views of the European Commission and/or the European Health and Digital Executive Agency (HaDEA) or any other body of the European Union.
The European Commission and the Agency do not accept any responsibility for use that may be made of the information it contains

Table of Contents

This report is part of the project "101056988/SUPPLY" which has received funding from the European Union's EU4Health Programme (2021-2027). The content of this report represents the views of the author only and is his/her sole responsibility; it can not be considered to reflect the views of the European Commission and/or the European Health and Digital Executive Agency (HaDEA) or any other body of the European Union. The European Commission and the Agency do not accept any responsibility for use that may be made of the information it contains

This report is part of the project "101056988/SUPPLY" which has received funding from the European Union's EU4Health Programme (2021-2027). The content of this report represents the views of the author only and is his/her sole responsibility; it can not be considered to reflect the views of the European Commission and/or the European Health and Digital Executive Agency (HaDEA) or any other body of the European Union. The European Commission and the Agency do not accept any responsibility for use that may be made of the information it contains

Role of this report

Donated plasma is the only source to produce plasma-derived medicinal products (PDMPs) which are indispensable for the treatment of patients with chronic conditions such as primary immunodeficiency, haemophilia and other coagulation disorders, and auto-immune neuropathies. European Union (EU) Member States (MS) have a responsibility to ensure safe and adequate access for EU patients to these essential PDMPs, including in cases where the supply tension situations for plasma present, or are likely to present, a serious risk to human health.

This report focuses on characterizing 4 types of crisis situation scenarios, specifically pandemic, war, climate change, and trade-war, that could significantly impact the availability of resources. The report highlights specific relevant outcomes from the SUPPLY project and additional items to be considered by stakeholders, both in preparing for, and dealing with, crises which arise.

The report is designed to inform, complement, and assist with EU and national plasma strategies, national SoHO emergency plans, and to coordinate with other response actions at national or EU level.

SUPPLY Project Description

The Covid-19 crisis has shown how vulnerable the world is in supply of life-saving medicines. Plasma-derived medicines, particularly immunoglobulins, are facing shortages in Europe today. Simultaneously, there is an imbalance in the global collection of plasma needed for the products, with a high dependence on plasma coming from the USA.

The SUPPLY project provides a set of recommendations and guidance to both increase plasma collection in the EU by the public health sector and to achieve optimal availability of plasma medicines for patients. The SUPPLY project therefore contributes to the EU becoming more strategically independent in its need for plasma medicines, aligning with the drive for wider EU strategic autonomy i.e. A reduced dependency on other countries in strategically important policy areas.[1]

This report is part of the project "101056988/SUPPLY" which has received funding from the European Union's EU4Health Programme (2021-2027). The content of this report represents the views of the author only and is his/her sole responsibility; it can not be considered to reflect the views of the European Commission and/or the European Health and Digital Executive Agency (HaDEA) or any other body of the European Union. The European Commission and the Agency do not accept any responsibility for use that may be made of the information it contains

Crisis Scenarios - Overview

The development of globalisation has made the EU acquire several dependencies on third countries. A recent non-paper[2], written by the Spanish Presidency of the Council of the European Union in close consultation with officials of the 27 Member States, the European Commission, the Secretariat of the Council of the EU, and several academics and private sector representatives, discusses some of the impacts of this globalisation, which was accompanied by an assumption in the EU that the open international order would be maintained indefinitely. This assumption led many European countries to outsource a significant portion of their economic activity and build global supply chains primarily based on relative cost criteria. The non-paper highlights the introduction of lower-priced US Plasma in 1993 under the newly-established European single market, with a subsequent reduction in the collection of plasma in Europe, as the definitive example of the EU acquiring risks through dependencies on third countries.

Recent crises confronted by the EU, such as those caused by the Covid pandemic, the Russian war against Ukraine, and an eruption in geopolitical tensions in the Middle East, have overlapped and amplified each-other. These crises have again exposed the significant risks of the EU's dependencies on third countries to the well-being of Europeans, with a reduction in the availability of plasma accompanied by shortages in PDMPs. An assessment of increasing geopolitical tensions, growing competition for some technologies and raw materials, and the impact of megatrends such as climate change and demographic ageing suggests that these vulnerabilities might worsen and multiply in the future.

These dependencies on third countries being revealed as serious vulnerabilities has led to an EU drive for "Open Strategic Autonomy" (OSA), loosely defined by the Council of the European Union as the "capacity to act autonomously when and where necessary and with partners wherever possible". In this context, and with the EU looking to protect its citizens from future external shocks, there is a move towards making the EU more strategically independent in its need for plasma medicine by focusing on increasing commitment and control over the plasma-PDMP-patient chain. It is of critical importance to implement requisite measures, including the recommendations in this report and the wider SUPPLY project, during periods of relative calm in most EU member states to ensure the plasma and PDMP system is robust and resilient in times of crises.

Crisis Situation Scenarios

1. Pandemic

The COVID-19 pandemic can be considered one of the biggest health crises that has affected Europe in our time. This crisis highlighted the vulnerabilities of the Union in very different aspects, ranging from the lack of coordination between Member States, which is essential to addressing such situations, to the Union's strong dependence on third countries for developing medical treatments[3].

SUPPLY | Co-funded by the European Union

This report is part of the project "101056988/SUPPLY" which has received funding from the European Union's EU4Health Programme (2021-2027). The content of this report represents the views of the author only and is his/her sole responsibility; it can not be considered to reflect the views of the European Commission and/or the European Health and Digital Executive Agency (HaDEA) or any other body of the European Union. The European Commission and the Agency do not accept any responsibility for use that may be made of the information it contains

The lessons learned and the resulting measures should serve as a reference for the prevention, detection and resolution of future health crises.

In the case of plasma, the pandemic drastically reduced the availability of plasma collected in the private sector or imported from third countries, putting the Union in a situation of shortages of PDMPs and patients at serious risk due to a lack of adequate treatments. The high prevalence of the covid disease in the population, physical distancing measures, and other restrictions on mobility led to a decline in plasma donations due to reduced donor availability, absenteeism of plasma collection staff, and perceived public fear of infection despite strong safety measures.

Pandemics inevitably result in unpredictable and uncertain environments, and many unforeseen outcomes emerged during the waves of the COVID-19 pandemic. Uncoordinated stockpiling and export restrictions confounded an increased demand for medicines used to treat patients. An increased demand for convalescent plasma for COVID-19 for investigational therapies posed an additional challenge to the plasma supply, particularly in the US.

The Covid-19 pandemic had an adverse impact on the resilience of the plasma donor base in some countries whose collection systems rely on a small number of persons donating SoHO more frequently than elsewhere, with the greater resilience of public, non-remunerated programmes emerging as a strong theme. Although commercial companies in the US increased the compensation per plasma donation during the pandemic in an effort to achieve pre-pandemic levels, the donor pool failed to meet demand, with US plasma volumes significantly lower in both 2020 and 2021. This is in marked contrast to the EU where countries running public non-remunerated plasma collection programmes had considerably less drops in donations, with some even increasing collections. The “headwinds” that continued to adversely impact paid-plasma collection volumes, as noted by commercial plasma-collectors, included the U.S. government financial assistance to assist economically vulnerable Americans, and the Mexican border and B1/B2 visa restrictions impeding donations in collection centres in close proximity to Mexico.

Pandemics may arise from pathogens that cause diseases where convalescent plasma and, often preferred as a more specific option, hyperimmunoglobulin preparations can offer a first line of acute treatment. This scenario was evaluated during the Covid pandemic, where both convalescent plasma as well as hyperimmunoglobulin products were tested. In the situation of the SARS-CoV-2 virus, with these studies being promoted at a late stage of the natural evolution of the disease, these treatment modalities were not found the most effective. It should be noted that beneficial aspects of the treatment for immunocompromised population are still under investigation by ongoing randomised studies.

Other pathogens and diseases can arise, however, and some planned responses include these sorts of treatments. If such a situation occurs, the use of convalescent plasma or a development of a new hyperimmunoglobulin preparation could be attractive. In such a case, rapid development includes both the donation of plasma rich in the antibody and the setting up rigorous testing methods and

SUPPLY | Co-funded by the European Union

This report is part of the project “101056988/SUPPLY” which has received funding from the European Union’s EU4Health Programme (2021-2027). The content of this report represents the views of the author only and is his/her sole responsibility; it can not be considered to reflect the views of the European Commission and/or the European Health and Digital Executive Agency (HaDEA) or any other body of the European Union. The European Commission and the Agency do not accept any responsibility for use that may be made of the information it contains

clinical protocols to evaluate the effectiveness. Consequently, if this proves a viable acute treatment option, extra efforts to increase plasma donation would be needed to ensure sufficient supply both for this new use and for the existing standard uses.

2. War

Scenario planning for future wars is very challenging[4]. Russia's war against Ukraine has caused substantial challenges to medicines supply chains in Ukraine as well as economic losses, while triggering one of the largest displacement crises on record in Europe since World War II, with the number of internally displaced people (IDPs) surpassing the 8 million mark in Ukraine in 2023.

Transportation challenges, both to and within Ukraine, have been the main risk identified to general pharmaceutical supply chains. Regarding the plasma product supply chain, however, the presence of a local PDMP fractionator means there has been a local supply, even in wartime. This is not often the situation in most European countries. So on this point, Ukraine could serve as a model for the importance of local/regional fractionation when other supply chain routes are blocked.

In terms of scenario planning for the impacts of future wars on the availability of both plasma and PDMPs, an additional consideration is a possible increase in the requirements for both blood and plasma for transfusion (in liquid, frozen, or lyophilised form). Again this need, and pressures on the existing donor pool, requires consideration along with the existing needs for Plasma for Fractionation (PfF), with planning to also include the potential stockpiling of critical medicines, such as PDMPs.

3. Climate Change

Climate change has the potential to cause major disruptions to the pharma supply chain and tragic health impacts for populations. Pharmaceutical supply chains are extremely vulnerable to the effects of climate change and face many challenges from sourcing to distribution. Volatile weather conditions, including soaring temperatures, extreme cold snaps, tornados, fires, and floods, can impact the plasma pharmaceutical logistics through ships being unable to leave ports, impact on infrastructures for power and water supply which immediately can hamper manufacturing, etc.[5] Similar impacts can arise from other natural disasters such as earthquakes. Additionally, climate change has a direct impact on population health[6], potentially increasing the demands for pharmaceutical products while the emergence of viral vectors (e.g. arbovirus transmission) which cause diseases can impact both the availability of donors and the safety of the products.

The EU's supply of plasma from the US is reliant on shipping. The recent European Maritime Transport Environmental Report, from the European Environment Agency and the European Maritime Safety Agency[7], shows that ships produce 13.5% of all greenhouse gas emissions from transport in the EU. Sulphur dioxide (SO2) emissions from ships calling in European ports amounted to approximately 1.63 million tonnes in 2019. Maritime transport is estimated to have contributed to the fact that

This report is part of the project "101056988/SUPPLY" which has received funding from the European Union's EU4Health Programme (2021-2027). The content of this report represents the views of the author only and is his/her sole responsibility; it can not be considered to reflect the views of the European Commission and/or the European Health and Digital Executive Agency (HaDEA) or any other body of the European Union. The European Commission and the Agency do not accept any responsibility for use that may be made of the information it contains

underwater noise levels in EU waters have more than doubled between 2014 and 2019 and has been responsible for half of all non-indigenous species introduced into European seas since 1949.

Acknowledging that if the climate change impact of shipping activities grows as projected, it will undermine the objectives of the Paris Agreement, the EU is taking several steps to significantly reduce greenhouse gas (GHG) emissions from international shipping. In January 2024, the EU's Emissions Trading System (EU ETS) was extended to cover CO2 emissions from all large ships (of 5000 gross tonnage and above) entering EU ports, regardless of the flag they fly. The legislation on the inclusion of maritime emissions in the EU ETS has been complemented by several implementing and delegated acts[8]. Noting that the demand for plasma is projected to rise at a compound annual growth rate of 9.4% until 2030 due to ageing demographics and the rising prevalence of immunodeficiency disorder, it is reasonable to assume that the contribution to plasma-linked GHG emissions from international shipping would similarly increase.

4. Trade-war

In an increasingly interconnected global economy, trade wars have emerged as significant threats to international trade and supply chains. Trade dynamics and geopolitical relationships can change over time, and the likelihood of a trade war can be influenced by various factors such as economic policies, trade negotiations, and political developments. Given the high trade intensity of the pharmaceutical supply chain, this sector is particularly sensitive to trade disputes.

Given the EU's current dependence on US plasma and the growing concentration and domination of global plasma supply by mainly US owners, disruptions caused by a trade war between the EU and US in particular could have far-reaching consequences for patients relying on PDMPs and for European healthcare systems in general. The high possibility of a return/commencement of a protectionist US administration which may weaponise US plasma exports makes this risk scenario very pertinent. The imposition of tariffs, trade barriers, or import and export restrictions would impede both the flow of plasma from the United States and, potentially, the procurement of necessary equipment and supplies for plasma collection. Inflationary pressures, job losses, and a substantial reduction in economic growth would exacerbate increased costs for European countries importing plasma[9]. These costs could trickle down to patients, healthcare providers, and national healthcare systems, straining budgets and potentially further limiting access to PDMPs.

Trade wars can hamper collaboration and knowledge sharing between countries. European countries rely on international research and development efforts for advancements in plasma-derived therapies. A trade war may disrupt these collaborations, impeding progress in scientific research and the development of improved and new plasma-derived products and supply chains. This disruption could have long-term implications for medical innovation and patient care.

SUPPLY | Co-funded by the European Union

This report is part of the project "101056988/SUPPLY" which has received funding from the European Union's EU4Health Programme (2021-2027). The content of this report represents the views of the author only and is his/her sole responsibility; it can not be considered to reflect the views of the European Commission and/or the European Health and Digital Executive Agency (HaDEA) or any other body of the European Union. The European Commission and the Agency do not accept any responsibility for use that may be made of the information it contains

5. Crisis Scenarios - Summary

We need to build resilience to deal with the complex cascading, cross-border, cross-sector impacts of crises. The following provides an overview of recommended actions, but it is highly advised to consult the relevant SUPPLY Deliverable reports where more detailed information is available.

It must be stressed that the EU is effectively dependent on one third country, the U.S., for plasma supply. This raises additional risks to the scenarios above including, but not limited to:

- Growing concentration and domination of global supply by mainly US owners or drivers of Plasma collection
- Emergence of US only/mainly unexpected transfusion-transmissible infections, like new infectious non-enveloped virus <15/20 nm
- Emergence of US only/mainly new infectious agent of unknown characteristics
- Commercial Consolidation
- Border control policy changes likely to negatively impact number of plasma donors travelling from Mexico particularly

This furthers strengthens the argument that possible diversification of this risk through additional suppliers, while building up EU plasma supply, is an important consideration.

The recommendations below focus mainly on plasma supply and PDMP usage, but crises will impact the availability of multiple resources which will impact the plasma-PDMP-patient chain, including human resources, financial resources, and equipment. To this end it is important that national emergency plans take account of these in the emergency planning sections of national plasma strategies.

Recommendations

Proactive Steps – European Union

The availability of PDMPs is dependent on both plasma collection and the involvement of different stakeholders identified at different steps of the provision process. Firstly, regional, national, and European authorities are central in defining legal frameworks for national plasma source procurement. It is crucial for policymakers, healthcare providers, and stakeholders to proactively address the risks identified above, but there are no silver bullets to solve the vulnerabilities in the donor-PDMP-patient chain of the EU. What is required is a systemic approach that combines different solutions and leverages the synergies between them.

SUPPLY | Co-funded by the European Union

This report is part of the project "101056988/SUPPLY" which has received funding from the European Union's EU4Health Programme (2021-2027). The content of this report represents the views of the author only and is his/her sole responsibility; it can not be considered to reflect the views of the European Commission and/or the European Health and Digital Executive Agency (HaDEA) or any other body of the European Union. The European Commission and the Agency do not accept any responsibility for use that may be made of the information it contains

1. **Legal provisions favouring collection of plasma as a strategic resource.**

The EU should adopt a common legislative framework in terms of principles aimed to define plasma as a strategic resource for the European citizens and to guarantee that plasma collected inside the EU gives origin to products which can secure the therapeutic benefit of the EU patients. The recommendations and outputs of the Critical Medicines Alliance, currently being established to address shortages of medicines, should be considered throughout.

2. **Legal provisions favouring cooperation among different systems and models.**

Public non-profit and private for-profit organisations play a role in blood and plasma collection in the EU, both for transfusion and for further fractionation into PDMPs. Efforts must be made to avoid both competition among the models and competition in the collection of plasma for fractionation among public and private for-profit sectors, promoting instead a cooperation toward the satisfaction of EU demand for plasma products in a sustainable way. This can be achieved by means of appropriate and specific legislative interventions aimed at securing a contribution of both private and public sectors to the priority satisfaction of national (or even European) demand of PDMPs.

3. **Legal provisions favouring cooperation among Member States (MS).**

The EU should help MS in creating legal environments that both eliminate any barrier against the pooling of plasma from different MS and promote the agreement among 2 or more MS (e.g., common toll manufacturing agreements or common tenders for selling plasma) in order to share a common approach on the fractionation of domestic plasma and the production and the return of strategic PDMPs.

4. **Priority use of products coming from fractionation of domestic plasma.**

The collection of EU plasma should be supported by adequate legal provisions ensuring that products coming from the fractionation of domestic plasma will meet a sustainable proportion of the national needs of patients for safe blood and blood products. Products coming from the fractionation of EU plasma are primarily intended to meet clinical demand for EU citizens. Interestingly, the US-FDA currently bans non-US plasma for the products authorised for the US market. However, it is in the interest of EU to be able to supply possible third countries with PDMPs when there are surplus products available. Also, with a strong fractionation capacity placed in EU, EU can provide substantial manufacturing service to third countries using their domestic plasma.

5. **Protect the current non-remunerated donor population.**

The current EU non-remunerated donor population ensures the continuous provision of 100% of the EU's needs in blood components other than plasma for fractionation and Europe is the largest global supplier of 'recovered plasma' for manufacturing into PDMPs. It is therefore of critical importance to

SUPPLY | Co-funded by the European Union

This report is part of the project "101056988/SUPPLY" which has received funding from the European Union's EU4Health Programme (2021-2027). The content of this report represents the views of the author only and is his/her sole responsibility; it can not be considered to reflect the views of the European Commission and/or the European Health and Digital Executive Agency (HaDEA) or any other body of the European Union. The European Commission and the Agency do not accept any responsibility for use that may be made of the information it contains

the availability of both PDMPs and critical SoHO that efforts to increase plasma collection do not erode the current non-remunerated SoHO donor population.

6. EU Supporting the increase and improvement of plasma collection

As of 2024, an estimated 65.6 Million EU Citizens have no access to a national plasmapheresis program. In order to support national and EU efforts to achieve a higher degree of strategic independence from non-EU sources, EU should launch and fund programmes aimed at increasing quantity and quality of plasma collected by BEs throughout Europe and ultimately strengthening the resilience of plasma collection.

7. Support prospective studies in plasma donors

There is a need to fund large, multi-centre clinical trials, and large data base linkage studies, to assess mid to long term donor health. This is of critical importance to maintaining donor health, of course, but also to ensure a comprehensive and planned response to the potential scenario of evidence emerging of significant donor risk, in particular in high frequency donors.

8. EU Plasma information and awareness campaigns

Campaigns at EU level to promote information and awareness on the importance of plasma donation are necessary and beneficial to all parties. The aim of these campaigns should be to ensure the broadest possible donor base with a view to a more resilient supply for plasma, and to help European citizens to decide whether to become plasma donors during their lifetime. These campaigns should be evaluated scientifically to optimize their impact over time. Account should be taken of further studies into the potential epidemiological benefits, in terms of the antibody repertoire, of a larger contribution of European sourced plasma into PDMPs used by European patients, and of the potential for harnessing the value of a 'European Identity' into information campaigns.

9. Develop a harmonised prioritisation and management plan for PDMP shortages

Since existing EU prioritisation plans and indications are not uniform between countries, a harmonised methodology is required as a first step to ensuring that each MS establishes a prioritisation plan for shortages of PDMPs. Integrating these plans with existing guidelines and recommendations through collaboration with relevant stakeholders, expert networks and scientific societies is crucial, and will enable linkages between similar initiatives for optimal synergy.

A harmonised management plan should include, inter alia:

- protocols on switching between brands and/or routing
- use of alternative treatments
- treatment paradigms

SUPPLY | Co-funded by the European Union

This report is part of the project "101056988/SUPPLY" which has received funding from the European Union's EU4Health Programme (2021-2027). The content of this report represents the views of the author only and is his/her sole responsibility; it can not be considered to reflect the views of the European Commission and/or the European Health and Digital Executive Agency (HaDEA) or any other body of the European Union. The European Commission and the Agency do not accept any responsibility for use that may be made of the information it contains

- best practices
- Europe-wide communication network and shortage awareness systems.
- a common backbone adaptable to each country's organization, epidemiology, and resources.

10. Important Projects of Common European Interest (IPCEI)

IPCEI in health are expected to cover the following: R&D in key therapeutic areas; process innovation, especially in the area of biologics; innovative and essential manufacturing activities in the field of bioproduction capacities, building spare, flexible capacity for pandemic situations; securing/increasing production capacity in medicines of key therapeutic interest; and strengthen digitalisation capabilities (for example, data management) across the health value chain. Investing in research and development to reduce dependence on PDMPs and/or to develop alternative therapies may provide long-term solutions.

11. Critical Medicines Alliance.

The EU's industrial policy should be implemented according to European, rather than national, logic. On the healthcare front, it is essential to reinforce the EU's supply chains, ensure access by all Member States to pharmaceutical products, and strengthen the joint procurement of medicines at an EU level, using the opportunity created by the Pharmaceutical Strategy.

The Critical Medicines Alliance is a consultative mechanism which brings together all relevant stakeholders to identify priorities for action and propose solutions to strengthen the supply of critical medicines in the EU, to better prevent and combat their shortages.

12. Develop a framework agreement for public-private collaboration

Litigation is a major obstacle to developing efficient tender procedures. Legal challenges can delay the availability of PDMPs from European plasma and can have a negative impact on sufficiency. It is time to assess and implement general agreements in public-private collaboration avoiding unnecessary and dangerous competition, which help to establish equitable procedures to guarantee the timely distribution of these products in a fair and just way for both parts. Therefore, the development of a framework agreement is recommended to help the resolution and smooth development of further specific tenders and agreements.

13. EU-level coordination of procurement

EU-level coordination of procurement should guarantee coordination between Member States to fairly allocate initially limited supply quantities in a transparent manner, and the need to prevent issues related to national distribution channels, or the risk of inefficient stockpiling. The initiative from the MSSG of the EMA on voluntary solidarity for medicinal products will also play a role here.

SUPPLY | Co-funded by the European Union

This report is part of the project "101056988/SUPPLY" which has received funding from the European Union's EU4Health Programme (2021-2027). The content of this report represents the views of the author only and is his/her sole responsibility; it can not be considered to reflect the views of the European Commission and/or the European Health and Digital Executive Agency (HaDEA) or any other body of the European Union. The European Commission and the Agency do not accept any responsibility for use that may be made of the information it contains

14. Training

The EU can play a role in training decision- and policy-makers to coordinate and manage crises.

15. Maritime Transport

Opportunities for aligning with the EU's efforts to significantly reduce greenhouse gas (GHG) emissions from international shipping should be assessed.

Similarly, opportunities to shape donor recruitment campaigns which include positive messaging on the reduction in GHG emissions associated with decreased reliance on US plasma should be considered.

Proactive Steps – Member State level

1. **Support the increase and improvement of plasma collection though National Plans.**

    a. Member States should increase their collection capacity and donor base for plasma by developing non-profit and public plasmapheresis programmes. Aligning with EU plans supporting the increase and improvement of plasma collection, the aim should be to ensure the broadest possible donor base, with a view to a more resilient supply for plasma. Member States should support the establishment of public donation facilities and promote the voluntary and unpaid donation of plasma, of high quality and safety. Tools for determining the optimal number of donor centres and their strategic location are available within the SUPPLY Deliverables.

    b. It is of critical importance that national commitments to collect sufficient volumes of plasma to meet the optimum plasma-related requirements of populations are accompanied by sufficient control and monitoring over the plasma-PDMP-patient chain, ideally through legislative guarantees, to ensure that the patient population needs are met.

    c. The European public donation system fulfils the needs of EU citizens regarding blood and blood products for direct transfusion. Efforts and initiatives to increase plasma collection must not erode the current non-remunerated donor population. SUPPLY revealed that the most successful countries, in terms of plasma donation recruitment programmes, are those that already had a significant number of whole blood donors who are referred to plasma donation as appropriate depending on the needs for red cells components.

    d. The following from the SoHO Regulation is relevant: 'In cases where the availability of critical SoHO or products manufactured from critical SoHO depends on potential commercial interests, such as those related to the production and distribution of plasma-derived products, there is a risk of not having the interests of patients and research at the forefront, and thus to jeopardise the quality and safety of SoHOs, their donors and their recipients. There could even be situations in which some products with low profitability

This report is part of the project "101056988/SUPPLY" which has received funding from the European Union's EU4Health Programme (2021-2027). The content of this report represents the views of the author only and is his/her sole responsibility; it can not be considered to reflect the views of the European Commission and/or the European Health and Digital Executive Agency (HaDEA) or any other body of the European Union. The European Commission and the Agency do not accept any responsibility for use that may be made of the information it contains

are no longer produced, thereby hampering their accessibility for patients. Hence, by considering all reasonable efforts for an appropriate and continuous supply of critical SoHO, Member States contribute to limiting the risk of shortages of products manufactured from critical SoHO.'

2. **Prioritise and resource Toll Fractionation / Contracted Service tender models**

Based on agreement for fractionation of domestic plasma and the subsequent return of PDMPs obtained, these models were frequently reported during SUPPLY as the preferred high-value tender model. These models motivate citizens to donate plasma for the implicit local benefit, enable the return of PDMPs to the country or region of origin ensuring traceability, and may demonstrate epidemiological benefits in terms of the antibody repertoire towards infectious diseases.

Additionally, these models can have a positive impact on social cohesion through its transparency, and on sustainability if economic savings are achieved or whether a significant impact on market prices is reached. Furthermore, these tender models align with the most recent Eurobarometer finding that 73-82% of respondents, both donor and nondonor, said they would be motivated to donate by the desire to help family, friends, and others in their communities.

SUPPLY also found that centralised tenders (Regional, National, or International) present possibilities for significant cost savings which can be reinvested in Plasma collection programmes, thereby advancing further towards the aim of ensuring that the patient population needs are met.

3. **Include protein yields, Ig content, and recovery percentages in tenders**

Although tenders and/or agreements take into account important factors such as protein manufacturing yields and/or recovery percentages, IgG content differs significantly between donations, and should be taken into account when tendering, noting that IgG content in European plasma pools with different background in donation frequency could differ by over 10% and 20-30%. More IgG can be recovered from high IgG concentration recovered plasma than from very high frequency (US) source plasma.

4. **Liaise with Blood Establishments and Invest in Plasma system improvements**

The SUPPLY consortium identified multiple opportunities for practical improvements to existing plasma systems, with a view to optimal use and minimal waste of donated plasma, both source and recovered. These recommendations are detailed particularly in SUPPLY Deliverables 3.1, 3.2, 3.3, 3.4, and 3.5.

SUPPLY | Co-funded by the European Union

This report is part of the project "101056988/SUPPLY" which has received funding from the European Union's EU4Health Programme (2021-2027). The content of this report represents the views of the author only and is his/her sole responsibility; it can not be considered to reflect the views of the European Commission and/or the European Health and Digital Executive Agency (HaDEA) or any other body of the European Union. The European Commission and the Agency do not accept any responsibility for use that may be made of the information it contains

5. **Invest in Plasma workforce**

    a. Challenges to the availability of skilled personnel could hinder the capacity to collect sufficient plasma locally during a crisis situation, further exacerbating the supply chain challenges. The plasma workforce faces similar challenges to those experienced by the broader health workforce, including, inter alia, shortages of staff, geographical inequalities, lack of specific training, changing technologies and care demands, and insufficient workforce planning. Member States must develop their own reforms according to the needs of the plasma system, to include planning for collection of sufficient plasma locally during a crisis situation.
    b. Transparency in communicating to citizens about the terms and conditions of tenders and agreements, and the foreseen, or already in place, formats of public-private collaboration is essential. In this sense, the appropriate training of staff involved in both the recruitment of plasma donors and plasma donation itself is essential to ensure accurate information is communicated to donors, thereby building and maintaining trust and loyalty.

6. **Create a harmonised national Ig database**

Being the driver for plasma collection, it is important to balance this demand with immunoglobulin (Ig) usage. To best measure Ig usage at baseline and in times of crisis, the creation of a harmonised national Ig database including a minimum dataset is necessary. Since MS do not have equal capacities to collect information about Ig use, short-term and pilot projects are required and feasible.

- Prerequisite - assess governance and responsibility regarding data jurisdiction, control, maintenance, accessibility, and sustainable resources.
- First step - identify existing data sources on Ig use within each MS, which includes established registries and databases from reference networks and scientific societies.
- Second step - collect patient data at a granular level. (A proposal of variables for both a *minimum* and an extensive dataset is provided in SUPPLY D6.2.)

7. **Establish and maintain communications amongst plasma stakeholders**

In those countries where a close relationship exists between the prescribers of Ig and other stakeholders in the plasma value chain, there is better management and insight on their use. This is a very important aspect to both achieving self-sufficiency and sustainability, and in times of crisis.

8. **National Plasma information and awareness campaigns**

Complementing the EU campaigns, campaigns at national level to promote information and awareness on the importance of plasma donation are necessary and beneficial. The aim of these campaigns should be to ensure the broadest possible donor base, with a view to a more resilient

This report is part of the project "101056988/SUPPLY" which has received funding from the European Union's EU4Health Programme (2021-2027). The content of this report represents the views of the author only and is his/her sole responsibility; it can not be considered to reflect the views of the European Commission and/or the European Health and Digital Executive Agency (HaDEA) or any other body of the European Union. The European Commission and the Agency do not accept any responsibility for use that may be made of the information it contains

supply for plasma, and help citizens to decide whether to become plasma donors during their lifetime. Account should be taken of further studies into the potential epidemiological benefits, in terms of the antibody repertoire, of a larger contribution of national sourced plasma into PDMPs used by citizens.

This report is part of the project "101056988/SUPPLY" which has received funding from the European Union's EU4Health Programme (2021-2027). The content of this report represents the views of the author only and is his/her sole responsibility; it can not be considered to reflect the views of the European Commission and/or the European Health and Digital Executive Agency (HaDEA) or any other body of the European Union. The European Commission and the Agency do not accept any responsibility for use that may be made of the information it contains

Recommended actions upon commencement of a crisis scenario

Decisions made during crises must balance urgency with long-lasting consequences, and therefore a longer-term perspective must be integrated within strategic crisis management. Important considerations when decision making during a crisis include quality assurance and risk management.

1. **Consult existing plans**

- National SoHO emergency and continuity of supply plans.

National emergency plans, as required under the SoHO Regulation, will include business continuity plans, detailed preparedness and response measures, supply chain resilience and supplier diversification options, stock-piling of certain SoHO where possible and appropriate, and arrangements for partnerships, including cooperation between SoHO competent authorities. At a SoHO entity level, it will be important to consult the relevant SoHO entity emergency plan.

- PDMP prioritisation and management plan

As described above, this should include protocols on switching between brands and/or routing, use of alternative treatments, treatment paradigms, best practices, and Europe-wide communication network and shortage awareness systems. Depending on the type of crisis, special emphasis may be needed for certain critical PDMPs such as hyperimmunoglobulins in pandemic situation or plasma for transfusion for bleeding, as well as albumin as a treatment of burns and as a volume expander in wartime.

2. **Communications**

- Emergency Response organisations:

Upon initiation of a crisis situation, it will be important to maintain close cooperation and consultation with health surveillance bodies, military medical services, civil protection services, and other services routinely involved in emergency responses. An assessment of needs should include consideration of demands, current and anticipated, on the available plasma, in addition to plasma for fractionation e.g. plasma for transfusion (liquid, frozen, lyophilised) etc.

- Manufacturing stakeholders

While the industrial fractionation capacity exists already within the EU to manufacture 100% of the volume and range of PDMPs currently required by EU patients, manufacturing stakeholders should be included in all communications upon initiation of a crisis situation, and should be involved in all task groups set-up during a crisis to ensure the donation-PDMP-patient pathway is streamlined.

SUPPLY | Co-funded by the European Union

This report is part of the project "101056988/SUPPLY" which has received funding from the European Union's EU4Health Programme (2021-2027). The content of this report represents the views of the author only and is his/her sole responsibility; it can not be considered to reflect the views of the European Commission and/or the European Health and Digital Executive Agency (HaDEA) or any other body of the European Union. The European Commission and the Agency do not accept any responsibility for use that may be made of the information it contains

- Patient representatives

Patient representatives are an important part of decision-making strategies and can make important contributions to the implementation of a simple and core set of criteria and actions.

- Immediate coordination with EMA's MSSG and SPOC Working Party.

The role of the European Medicines Agency's (EMA) 'Medicine Shortages Steering Group' (MSSG) is to ensure a robust response to medicine supply issues caused by major events or public-health emergencies. It coordinates urgent actions within the EU to manage medicine supply issues and issues related to the quality, safety and efficacy of medicines.

EMA's Single Point of Contact (SPOC) is the WP of the MSSG, and can facilitate effective coordination with the national competent authorities.

- Coordinate with/assess recommendations of CHESSMEN Project

The Coordination and Harmonisation of the Existing Systems against Shortages of Medicines – European Network (CHESSMEN) project is a project aiming to support European MS to provide a harmonised response to mitigate medicines shortages and to contribute to an appropriate and timely availability of medicinal products.

- Donor Representative Organisations

Initiation of a crisis will necessitate a rapid/urgent mobilisation of Plasma Donors. It is recommended that Donor representatives via the international federation of blood donor organisations FIODS/IFBDO are included in tailoring European-wide messaging, which can complement regional and national initiatives.

- Public Notifications and civil society involvement

As disruptions in source plasma pipelines, and the potential impacts on health, may not be readily perceived by many stakeholders in the plasma value chain or indeed the wider public, an immediate public awareness campaign is recommended, ideally coordinated and managed at both European and MS level.

The Scientific Advice Mechanism, which provides independent scientific evidence and policy recommendations to the European institutions by request of the College of Commissioners, notes that crises amplify existing inequalities, hitting the most vulnerable the hardest — and this can erode trust across society at exactly the time when trust is most needed. Involving civil society can bring many advantages, producing a better informed, tailored, and localised response from engaged and empowered EU citizens.

This report is part of the project "101056988/SUPPLY" which has received funding from the European Union's EU4Health Programme (2021-2027). The content of this report represents the views of the author only and is his/her sole responsibility; it can not be considered to reflect the views of the European Commission and/or the European Health and Digital Executive Agency (HaDEA) or any other body of the European Union. The European Commission and the Agency do not accept any responsibility for use that may be made of the information it contains

3. **Test, review and optimise donor recruitment and retention strategies targeted to donor segments**

It is important to keep a larger donor base and recruit sufficient donors. The large majority (14 of 17) of organisations surveyed in SUPPLY had to adapt their recruitment strategies during the COVID-19 pandemic. Many organisations moved from face-to-face recruitment to more online campaigns (e.g., social media, using influencers). Additional items to consider are using new or different media, targeting new or different audiences, and/or forging new collaborations with other organizations, authorities, and companies.

While SUPPLY found that it is more cost efficient to focus on retaining plasma donors and increasing their frequency, this needs to be re-assessed during a crisis, noting that the donation frequency decreased during the Covid-19 pandemic.

Unlike recruitment strategies, retention strategies were largely unchanged during the pandemic in the majority of respondents during SUPPLY.

4. **Comprehensive Funding Response to the crisis**

Maintaining responsive and flexible funding during a crisis can ensure help that existing and novel plasma supply initiatives are progressed, support networks of experts are maintained, valid and relevant scientific and technical questions are answered, and research proposals continue to be reviewed in an expert and timely manner.

5. **Ensure continuous protection of plasma donors and SoHO recipients**

It is anticipated that, to ensure supply of critical SoHO, including plasma, Member States may allow for derogations from certain standards and obligations set out in the SoHO Regulation when large scale life-threatening situations in the context of man-made or natural disasters, notably in the context of armed conflicts, pose a risk to human life. It is also anticipated that such derogations shall not be granted from the provisions of the Regulation that concern voluntary unpaid donation and plasma donor consent, and that the derogations shall be applied in a manner that ensures the protection of SoHO donors and SoHO recipients to the maximum extent possible in the circumstances of the crisis.

Monitoring Indicators

It will be critical to monitor PDMP trends and availability, particularly Ig, and appropriate clinical utilisation. The national Ig database should serve as the foundation, and a proposal of variables for an extensive dataset is provided in SUPPLY D6.2.

SUPPLY | Co-funded by the European Union

This report is part of the project "101056988/SUPPLY" which has received funding from the European Union's EU4Health Programme (2021-2027). The content of this report represents the views of the author only and is his/her sole responsibility; it can not be considered to reflect the views of the European Commission and/or the European Health and Digital Executive Agency (HaDEA) or any other body of the European Union. The European Commission and the Agency do not accept any responsibility for use that may be made of the information it contains

Key performance indicators for use in crisis scenario planning, management, and recovery will also include continuous monitoring of all activity data at regional, national, and EU level concerning plasma activities (collection [both source and recovered], distribution [including, inter alia, PfF, direct for transfusion, convalescent plasma, lyophilised, and use in reagent preparation], import, and export. SoHO competent authorities must be in a position to get an overview of the availability of plasma and PDMPs in their territories when needed.

It is proposed to use the EU SoHO Platform, the digital platform to facilitate the effective and efficient exchange of information concerning plasma activities in the EU, as provided for in the SoHO Regulation, as the secure channel for restricted exchange of the relevant information and data. This should allow regional, national, and EU level assessment of the agreed KPIs, and enable information to be exchanged between relevant stakeholders, as appropriate.

Summary

It is impossible to fully identify all risks and threats which may arise from the crisis situations described above. The effects of overlapping crises with growing complexity can cascade and ripple to all parts of society, the economy, and the environment. The effects of such crises are not limited to specific geographical regions or sectors of society, and many crises continue indefinitely.

Plasma is a critical medical raw material and a public resource that requires strategic management. It is of critical importance that national commitments to collect sufficient volumes of plasma to meet the optimum plasma-related requirements of populations are accompanied by sufficient control over the plasma-PDMP-patient chain, ideally through legislative guarantees, to ensure that the patient population needs are met, including in times of crises. Achieving EU strategic autonomy in plasma will require a common vision, political will, and capabilities to implement it, and the collaborative efforts of all stakeholders.

This report is part of the project “101056988/SUPPLY” which has received funding from the European Union’s EU4Health Programme (2021-2027). The content of this report represents the views of the author only and is his/her sole responsibility; it can not be considered to reflect the views of the European Commission and/or the European Health and Digital Executive Agency (HaDEA) or any other body of the European Union. The European Commission and the Agency do not accept any responsibility for use that may be made of the information it contains

References

See SUPPLY Project Deliverables for relevant references. Additional sources used for this report include:

1. EU strategic autonomy 2013-2023 From concept to capacity www.europarl.europa.eu/RegData/etudes/BRIE/2022/733589/EPRS_BRI(2022)733589_EN.pdf

2. ResilientEU 2030: https://futuros.gob.es/sites/default/files/2023-09/RESILIENTEU2030.pdf

3. Supply Chains reshaping - How to respond to a crisis https://www.efpia.eu/news-events/the-efpia-view/blog-articles/supply-chains-reshaping-how-to-respond-to-a-crisis/

4. NATO – Relations with the EU https://www.nato.int/cps/en/natohq/topics_49217.htm

5. The impact of climate change on the pharma supply chain The-impact-of-climate-change-on-the-pharma-supply-chain.

6. Strategic crisis management in the EU https://sapea.info/topic/crisis-management/

7. European Maritime Transport Environmental Report 2021 https://www.eea.europa.eu/publications/maritime-transport/

8. EU - Reducing emissions from the shipping sector https://climate.ec.europa.eu/eu-action/transport/reducing-emissions-shipping-sector_en

9. Shortage of plasma-derived products: a looming crisis? Shortage of plasma-derived products: a looming crisis? | Blood | American Society of Hematology

This report is part of the project "101056988/SUPPLY" which has received funding from the European Union's EU4Health Programme (2021-2027). The content of this report represents the views of the author only and is his/her sole responsibility; it can not be considered to reflect the views of the European Commission and/or the European Health and Digital Executive Agency (HaDEA) or any other body of the European Union. The European Commission and the Agency do not accept any responsibility for use that may be made of the information it contains