PLUS
PLATFORM OF PLASMA PROTEIN USERS

FUTURE ACCESS TO PLASMA DERIVED MEDICINAL PRODUCTS: PATIENT CENTERED DECISION MAKING

29th September 2020
15:00-16:30 CET

Online Event

In collaboration with
MEP Sirpa Pietikäinen
(EPP)

epp group
in the european parliament

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1. Introduction

On Tuesday 29 September 2020, the Platform of Plasma Protein Users (PLUS) organised, in collaboration with MEP Sirpa Pietikäinen (EPP, Finland), an event entitled "*Future access to PDMPs: Patient centred decision making*". The event, moderated **by Dr. Jacqueline Kerr, from the Paul-Ehrlich-Institute**, and **Brian O'Mahony, from the Irish Haemophilia Society**, called for a patient centred approach in future decision-making around the need for plasma and access to Plasma Derived Medicinal Products (PDMPs).

Following the publication of the European Commission's final evaluation on the EU Blood, Tissues and Cells (BTC) legislation on 11 October 2019 and the meeting of the Committee on the Environment, Public Health and Food Safety on 3 December, EU institutions' work on the BTC legislation will increase. In fact, according to the 2021 Work Programme of the European Commission, the revision of the BTC legislation is planned for Q4 2021, and will also be accompanied by an Impact Assessment prior to that.

In this context the event triggered a patient centred discussion on how to address the various shortcomings in the current policy framework, and demonstrated the current challenges facing patients with regards to achieving a sustainable supply of PDMPs to meet patient needs.

2. Opening Remarks

PDMPs are products prepared from human plasma, including life-saving therapeutics for several chronic and acute life-threatening diseases. Grasping the full benefits of PDMPs requires overcoming multiple challenges to optimal patient access. In the EU, these challenges include sufficient supply of plasma to meet the health needs of patients, ensuring the availability of safe PDMPs, and ensuring cooperation between the blood and plasma sectors. These are the points highlighted by Dr. Kerr and Mr. O'Mahony during their introductory remarks. As a PLUS representative, Mr. O'Mahony noted that PLUS gathers on a yearly basis to discuss these pressing issues for the patient community. He further highlighted the positive impact of the BTC legislation on the quality and safety of blood components. Unfortunately, in the context of the current pandemic and other events, plasma supply is at risk in the EU and there is a need for a solution to ensure access to a sustainable supply of PDMPs for patients whose lives rely on these life-saving treatments. For this reason, activities around the BTC legislation are of utmost importance for the patient community.

Following the brief introduction from the moderators, **MEP Sirpa Pietikäinen (EPP, Finland)** formally opened the event. As a politician, Ms. **Pietikäinen** has been a long-term supporter of PLUS' members and she noted that while the topic of access to PDMPs is not new, the current issues around it are. She highlighted that products for patients need to be safe, accessible, and available and further explained

that there are broad problems with access to PDMPs. The current unprecedented context of the pandemic is also raising concerns of potential plasma shortages. She also referred to the BTC legislation, noting that a review is in preparation by the European Commission. Work on the BTC however, requires the active input of patients and all relevant stakeholders so that politicians can adopt policy measures that ensure proper access and adequate resources allocated at EU level.

3. Patients' challenges

The first panel was an active discussion with patient representatives on addressing specific challenges faced by patients in terms of access to PDMPs. The panel included Otilia Stanga (Chair of the Romanian Patient Organisation for Primary Immunodeficiencies – ARPID), Declan Noone (President of the European Haemophilia Consortium) and Frank Willersinn (founder and President of the Belgian patient-driven organisation Alpha-1 Plus).

In her interaction with the moderator, Otilia Stanga emphasised that providing access to PDMPs is essential to improve the lives not only of patients but also of their families and communities. She noted that although PDMPs are often associated with rare diseases, it is estimated that 1 out of 5 people will need such products at least once in their lifetime. She further elaborated on the immunoglobulin shortage crisis in Romania in 2017-2018, which severely affected PID patients. This crisis was due to several factors such as a deficient price mechanism and lack of public engagement. The bottom line was that approximately 10% of PID patients chose to leave Romania due to this lack of treatments. Other patients' health, employment and personal finances were severely affected. A movie about the issue was also produced and is available here. It illustrates the problems patients are facing from not having proper and continuous access to PDMPs.

Declan Noone, from the European Haemophilia Consortium, stressed that blood and plasma collection is a very complex and multifaceted topic. In this light, patients' involvement in policymaking is essential for comprehensive care across all aspects of the treatment pathway – from donors to patients. In terms of plasma supply, Mr. Noone stated that currently, a large part of Europe's supply comes from non-EU sources and thus Europeans are dependent on third parties. He noted that politically, following declarations such as the Dublin consensus[1] is key to ensure improved plasma collection and improved patient access while ensuring that Member States' efforts are complementary rather than competitive.

The last member of the panel to exchange views with the moderator was Dr. Frank Willersinn from Alpha-1 Plus. In his intervention, he specifically noted that Alpha-1 is underdiagnosed by 90% in Europe. On top of this, Alpha-1 patients depend highly on PDMPs for treatment, and it is estimated that nearly **900 donations are needed to treat 1 patient per year**. Improving plasma management and increasing the donation of plasma are therefore key in ensuring security for Alpha-1 patients. Dr. Willersinn highlighted that in Europe, there is a need to ensure sustainable supply of PDMPs. The EU must recognise this as a main issue for rare diseases in terms of public health policy.

Two main points, highlighted by all three patient representatives, stood out during this interactive discussion:

1. In Europe, there is a high need for a sustainable supply of PDMPs.
2. The EU needs to recognise rare diseases as a main issue for public health policy.

[1] B. O. Mahony & A. Turner (2010). *The Dublin Consensus Statement on vital issues relating to the collection of blood and plasma and the manufacture of plasma products*. 2010 version available at https://onlinelibrary.wiley.com/doi/abs/10.1111/j.1423-0410.2010.01310.x; and 2011 version available at https://pubmed.ncbi.nlm.nih.gov/21806632/

4. Panel discussion with patients and experts on sustainable access to safe PDMPs

The event continued with a panel discussion with patients and experts on sustainable access to safe PDMPs. This panel, moderated by Dr. Kerr, featured Dr. Matthew Hotchko, President of the Marketing Research Bureau (MRB), Johan Prevot from the International Patient Organisation for Primary Immunodeficiencies and PLUS, Dr. Dragoslav Domanovic from the European Centre for Disease Control and Prevention (ECDC) and Dr. Guy Rautmann from the European Directorate for Quality of Medicines (EDQM) of the Council of Europe.

The discussion started with an overview of the current situation of plasma donations across Europe. Dr. Hotchko described the different systems currently in place. Different countries in Europe have different approaches to collect plasma for therapeutic or fractionation use, but there are two main categories.

1. Countries which rely on a government entity or non-profit organizations to collect all of the plasma used both for transfusion, as well as sent for fractionation into purified plasma proteins. This is the most common approach used in Europe, adopted by countries such as France, Italy and Spain. Under this system, donors are not monetarily compensated.
2. Countries where plasma to be used for transfusion is collected by government or non-profit organizations, while plasma to be sent for fractionation into plasma derived products is collected either by non-profit organizations or mainly by commercial companies. This approach is taken by just four countries in the European Union, namely Germany, Austria, Czech Republic and Hungary. Those who donate source plasma to be used for fractionation are customarily given monetary remuneration, though often modest, while those that donate whole blood are given the same types of non-monetary compensation seen in countries not offering commercial source plasma donation.

Dr. Hotchko noted that countries that allow private apheresis collection with monetary compensation collect over 3 times as much plasma for fractionation per resident than those that only have government or non-profit plasma collections systems, and thus even export the plasma surplus . He also stated that the countries which only have non-profit sectors fail to collect enough plasma to meet the needs of their patients when it comes to immunoglobulin usage. For example, in 2017, MRB data suggested that France needed to collect 1,650,00 more liters of source plasma to satisfy the needs of its immunoglobulin patients. That is an increase of 185% of the collected among in that same year. Meanwhile, Spain needed to collect an additional 588,000 liters, an increase of 57%, and Italy to collect 378,000 more liters, an increase of 45%. The deficit in 2019 and today is even greater than the 2017 numbers, as immunoglobulin demand has been rising faster than plasma collection in these three countries.

The conclusions from Dr. Hotchko's intervention was that nearly all countries which do not allow private apheresis plasma in the European Union have a shortage of plasma to meet the needs of their own immunoglobulin patients. These countries therefore rely on products made from compensated American donors, as the United States supplies about two-thirds of the entire plasma used for fractionation in the world. In the present circumstances of the global coronavirus pandemic, plasma collection in the United States has fallen sharply since March. This would lead to a shortage of plasma and affect all immunoglobulin patients, particularly those that rely on these imported products, as there will be less plasma exported from the United States in 2020 and early 2021 than in previous years.

Johan Prevot, from the International Patient Organisation for Primary Immunodeficiencies (IPOPI) spoke of the core PLUS principles and emphasised that supply has become the main safety issue for patients dependent on PDMPs. PLUS calls for:

1. Increased supply and free movement of safe and efficacious PDMPs developed on robust GMPs to meet patients' growing needs.

2. Development of guidelines, policy & legislation should be based on **FACTS & SCIENCE** & experience (not ideology).
3. Safety of patients means global sufficiency based on regionally balanced plasma collection (each region has to do more, incl. the EU).
4. Avoid wastage of plasma.
5. Develop or strengthen plasmapheresis programmes when possible.
6. Encourage the co-existence of public & private plasma collection to face the needed investments and benefit from existent knowledge and experience.
7. Future EU legislation on PDMPs should be **patient-centred**.

Mr. Prevot also noted that it is likely that COVID-19 would affect PDMPs supply. There are current discussions on the extent to which the current pandemic could affect blood and plasma donation, although it is evident there has been a decline in plasma collection since the beginning of the pandemic. Mr. Prevot highlighted Commissioner Kyriakides' statement for World Blood Donor Day, where she unprecedentedly referred to the role of plasma donors[2]. PLUS calls for an open and transparent dialogue with EU stakeholders on potential plasma shortages.

In his intervention with the moderator Dr. Domanovic, from the ECDC, highlighted that the centre reacted quickly to the threat posed by COVID-19 and produced recommendations, as well as comprehensive technical documents, which have been updated several times since then[3]. Donors may also be at increased risk of COVID-19, and thus staff should be informed and educated to ensure appropriate hygiene is respected, following national guidance. He noted that the assessment of the supply of substances of human origin (SoHO) has not been completed as the pandemic is still ongoing. Challenges identified to date include reduced donor and staff availability, and limited provision or distribution of critical materials and products. The European Medicines Agency (EMA) is expected to publish the results of a survey on EU Masterfile donors in 2020 which will provide more insights into future trends.

Dr Guy Rautmann, from the EDQM, explained the activities of the Directorate to improve plasma sustainability and access to PDMPs. He referred to the creation of a plasma supply management working party. The main task of this party is to determine how to use recovered and source plasma to its full potential. Surveys and stakeholder contacts are being carried out to understand the EU landscape on available plasma. The party held meetings in 2015 with representatives from different stakeholder groups, including patients and donors. It was concluded that the best way to tackle these issues is through a symposium, which was organised alongside DG SANTE in January of 2019 and was the first time such a complete dialogue on this subject took place. He concluded that the EU needs to investigate effective, pragmatic, and science-based models of blood and plasma donations to make a difference with supply.

Based on the interventions from the different panellists, it was evident that the EU needs to develop effective models of collection of blood and plasma. The dependency on the US is something which cannot be overlooked, especially given that sufficient supply of PDMPs for patients is increasingly at stake.

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[2] European Commission, *World Blood Donor Day: Statement by Commissioner Kyriakides*. Available at https://ec.europa.eu/commission/presscorner/detail/en/STATEMENT_20_1062

[3] European Centre for Disease Prevention and Control. *Coronavirus disease 2019 (COVID-19) and supply of substances of human origin in the EU/EEA*. Available at https://www.ecdc.europa.eu/en/publications-data/coronavirus-disease-2019-covid-19-and-supply-substances-human-origin

5. Political panel discussion

Following the discussion with experts, Dr. Kerr started the political panel discussion. This panel aimed to provide a political perspective on access to PMDPs. The panel included Sebastian Rohde, founder and senior advisor at RPP, Dr. Stefaan van der Spiegel, Head of Sector on Health Innovation at DG SANTE and MEP Sirpa Pietikäinen (EPP, Finland).

The discussion started with a brief political background on the BTC legislation which was provided by **Mr. Rohde**. Mr. Rohde provided the political context on the EU's approach towards blood & plasma since the late 90s. He noted that the EU's blood legislation was first established at a time when Member States had little will to transfer competences on Public Health to the EU. Nonetheless, there was a need for minimal standards for blood collection. He emphasises that the blood directive from 2002, should be seen as a "minimal standards" directive. This directive also provoked a political debate on the issue of compensated donation of blood derivatives, such as plasma. As no compromise was reached, the directive allowed for Member States to proceed as they see fit in this regard. Mr. Rohde also spoke about other debates which arose from the Blood directive such as:

- Whether self-sufficiency should be regarded as a national or EU level issue
- Deferrals of donations from men who have sex with men (MSM)
- New pathogens in the EU

It would be opportune to observe if these topics would be addressed in the potential upcoming revision of the Blood directive.

Following this background presentation, **Dr. Van der Spiegel** mentioned that an open public consultation will be included in any future legislative work on the BTC legislation. He specifically noted that the Commission counts on PLUS members to ensure the continuation of this dialogue with patients. The overall findings of the evaluation to the Blood Directive from 2019 were that the legislation has indeed improved safety and quality. Dr. Van der Spiegel also recognised that the EU is unfortunately dependent on plasma from the United States. One third or more of PDMPs for EU patients originate from US sources, which may lead to possible supply disruptions in case of crisis such as the current pandemic. **He noted that the European Commission monitors this closely, alongside the EMA**. As of September 2020, while some reductions of plasma collection were seen, there were also reports of increased plasma donation in other areas, and Plasma Master File (PMF) certificate holders have reported foreseen stocks and contingency plans. Dr. Van der Spiegel informed participants that there will be another survey with PMF holders to ensure a close monitoring of the situation. Nonetheless, the issue of supply has been put on the political agenda to achieve sufficient and safe supply in the future. He agreed to keep stakeholders informed of the progress of the Inception Impact Assessment (IIA) on the blood directive, which is being prepared by the European Commission. No specific timeline was discussed.

MEP Pietikäinen emphasised that addressing concerns of patients is of high priority in the European Parliament. Regarding monetary compensation, policymakers are often concerned about creating a bias where less privileged populations will be unfairly targeted for donations through this system. She noted that this needs to be addressed to ensure the rights of donors' standards are upheld, while also increasing the number of safe donations to ensure continuity of supply for patients. A better understanding of discrimination within donation, such as regarding vulnerable people, or the issue of donations from MSM, is also crucial. Ms. Pietikäinen ended her intervention by stating that she is open to continuing the discussion with patient groups.

6. Concluding remarks

Brian O'Mahony emphasised that Europe needs to act quickly and start collecting plasma independently and contribute to the global plasma supply. He stated that there is a need to develop a concrete plan to address the issue of global PDMPs supply. Decisions need to be based on science and patient needs and protect donors, and not on ideology. He also reflected that the previous blood directive referred to donors 43 times but only mentioned patients three times. He concluded by stating that patients need to be an integral part of the decision-making process. He hopes to see a change in this in the future, as these donations are mainly done for the benefit of the patients. Lastly, he informed participants that PLUS is developing a set of political recommendations based on the discussions which took place.

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LIST OF PARTICIPANTS

Panellists

- Dr. Jacqueline Kerr, Paul-Ehrlich-Institute
- Brian O'Mahony, Irish Haemophilia Society
- Sirpa Pietikäinen, Member of the European Parliament, EPP, Finland
- Otilia Stanga, Romanian Association for Patients with Primary Immunodeficiencies (ARPID)
- Declan Noone, European Haemophilia Consortium (EHC)
- Frank Willersin, Alpha-1 Plus
- Matthew Hotchko, Marketing Research Bureau
- Johan Prevot, International Patient Organisation for Primary Immunodeficiencies (IPOPI)
- Dr. Dragoslav Domanovic, European Centre for Disease Control (ECDC)
- Dr Guy Rautmann, European Directorate for the Quality of Medicines & HealthCare (EDQM)
- Sebastian Rohde, RPP
- Dr. Stefaan Van der Spiegel, DG SANTE, European Commission

Attendees

- Alexandra Marcinko, European Parliament
- Aline Mola, RPP
- Andrea Gressani, AIP odv
- Anneli Larsson, Primär immunbristorganisationen (PIO)
- Bianca Piantanida Pizzera, AIP, IPOPI
- Birgit Schlennert, DSAI e.V.
- Charles Waller, RPP
- Charline Quillérou, RPP
- Constantin Radu, Romanian Health Observatory
- Debbie Hum, World Federation of Hemophilia
- Dominika Misztela, Regulatory Policy Europe, Plasma Protein Therapeutics Association (PPTA)
- Dr. Nizar Mahlaoui, IPOPI
- Elliot Tricot O'Farrel, RPP
- Fernanda Ferro, Alpha-1 Plus
- Francesca Catassi, RPP
- Giancarlo Pineiro, Alpha-1 Global
- Jean-Philippe Plançon, European Patient Organisation for dysimmune and inflammatory neuropathies (EPODIN)
- Jose Drabwell, IPOPI
- Julia Nordin, IPOPI
- Kyriakos Nikopoulos, RPP
- Laura Pätsi, European Parliament
- Laura Savini, EHC
- Leire Solis, IPOPI
- Lisa Laumen, European Parliament
- Magda Lourenço, Communications Manager, IPOPI
- Marie Frostin, EFS
- Martin Balbachewski, RPP
- Nastassia Kisialeva, EHC
- Patricia Blomkwist-Markens, GBS|CIDP Foundation International
- Randel Plant, Alpha-1 Foundation
- Robert Perry, IPFA
- Stijn Willems, European Parliament
- Susanna Louhimies, Patient organisation
- Victor Sole, European Parliament
- Yordan Aleksandrov, RPP

I. ANNEX I: QUESTIONS AND ANSWERS

1. Charles Waller, Plasma industry consultant, mentioned that the UK is using convalescent plasma from recovered COVID patients. In this regard, he asked if UK plasma would be good enough to treat British newly infected COVID patients, would it this mean it would be also good enough for PDMPs?

   - **PLUS** stresses that there is a definite need to seriously reconsider the suitability of UK plasma for fractionation. Decisions should be taken based on science and evidence whilst taking into account the context of growing national and global need. The costs have been high in terms of opportunity, loss of fractionation capacity, and supply shortages. In the context of COVID-19, and whilst the UK is collecting convalescent plasma, such collection could have been more efficient and timely had an existing national plasmapheresis collection system already been in place.

2. Jose Drabwell, IPOPI, asked whether it would be possible to have a collaboration between plasma fractionators and convalescent plasma collectors to increase plasma supplies, including representatives from the Member States and PLUS. She also asked if PDMPs would be included in the EU pharmaceutical strategy as it aims to deliver safe and affordable medicines to patients.

   - The Communication on the pharmaceutical strategy aims at proposing measures to improve access and availability of all concerned medicinal products. The plasma derived medicinal products are not excluded at all from the scope of this initiative.

3. Susanna Louhimies, an Alpha-1 patient, referred to reimbursement as an issue of accessibility. She stated that harmonisation of reimbursement for plasma-based products across the EU, especially in rare diseases, is needed. These issues of accessibility also add a mental burden to those suffering due to such diseases. She asked whether the European Parliament has considered addressing this problem or would do so in upcoming discussions.

   - As discussions in the European Parliament are at an early stage, specifics have not been discussed. That being said, MEPs, including MEP Sirpa Pietikainen are open for continuing the dialogue with patients.

4. Jean-Philippe Plançon, chair of the European Patient Organisation for dysimmune and inflammatory neuropathies (EPODIN), mentioned the need for a coexistence of private and public systems. He noted that the question of compensation in Europe must undoubtedly be put into perspective with the acceptable number of donations per person per year. A sustainable system for patients must also consider the wellbeing of the donors.

   - Otilia Stanga highlighted as well that Romania remains a country that does not collect plasma for PDMPs, despite ARPID's efforts in this regard. She stated that it would be necessary for each country to collect plasma in an amount consistent with the estimated need. This is difficult to achieve in some countries, and thus a single legislative framework, monitored at European level, would be essential.