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DIRECTORATE-GENERAL FOR HEALTH AND FOOD SAFETY

Directorate B - Health systems, medical products and innovation
B4 – Medical products: quality, safety, innovation

Brussels, SANTÉ/DF

Stakeholder Workshop with Blood Competent Authorities

Substances of Human Origin Expert Group (CASoHO E01718)

4 May 2021, 09:30-13:00
By teleconference

WORKSHOP TOPIC: Regulating for Sufficiency – blood and plasma

Summary Minutes

Participants: All EU blood competent authorities were invited to this workshop and all, except Belgium, were in attendance. Liechtenstein, Montenegro, Norway, Republic of North Macedonia, Serbia and Turkey also attended as well as representatives of the Council of Europe (EDQM), ECDC and EMA.

The following stakeholder organisations attended: European Blood Alliance (EBA), European Plasma Alliance (EPA), Plasma Protein Therapeutics Association (PPTA), International Plasma Fractionators Association (IPFA), the International Patient Organisation for Primary Immunodeficiencies (IPOPI), European Patient Organisation for Dysimmune and Inflammatory Neuropathies (EPODIN), the European Haemophilia Consortium (EHC), the International Federation of Blood Donor Organisations (IFBDO), and the European Hospital and Healthcare Federation (HOPE). The Standing Committee of European Doctors (CPME) and the European Patients' Forum (EPF) had sent apologies.

1 WELCOME AND INTRODUCTION OF STAKEHOLDERS PRESENT

The DG SANTE B4 Head of Unit opened the workshop, welcoming all of the authorities and stakeholders. He explained that the event was organised in the context of the Impact Assessment for the revision of the BTC legislation. The objective was to provide an opportunity for key stakeholders in the blood and plasma fields to present, to the national blood competent authorities and the Commission, their positions on the topic of ensuring a sustainable supply of blood and plasma. It was explained that the format would be that of a 'hearing' rather than an interactive discussion. The views expressed would form part of the evidence gathering process for the Impact Assessment.

He explained that the authorities would have the opportunity to ask questions, to clarify their understanding and to indicate, in an anonymous manner (using online polling), their initial reactions to the proposals made by stakeholders.

Authorities were informed that closed meetings of each competent authority group (blood and tissues & cells) were scheduled for June to discuss openly the topics that will have been explored in all three hearings being organised by the Commission and the 11 stakeholder workshops being organised by the contractor, ICF.

2 INTRODUCTION TO THE WORKSHOP – DG SANTE

DG Santé summarised the topic of the hearing, explaining that it addressed one of the key five shortcomings identified in the BTC evaluation, i.e. the lack of legislative measures to support the achievement of a sufficient and sustainable BTC supply. It was noted that the key legislative measures identified were (i) the introduction of regular supply monitoring at a national and EU level, and (ii) the introduction of requirements to have emergency plans in place. It had been noted also that having the possibility for more regulatory flexibility could support increased supplies during crises that threaten sufficiency. It was noted also that non-legislative measures such as increased collection and improved utilization could be supported by the European Commission in other ways. It was underlined that this workshop would focus on the possible legislative measures.

DG Santé informed the participants that there had been a high level of response to the public and targeted online consultations, with submissions from across the EU and from all affected sectors and stakeholder groups. It was notable that a majority of respondents were working across the blood and tissue and cell fields, and many worked also in related fields, particularly pharmaceuticals. Some preliminary results were presented for those consultation questions that touched on the topic of this hearing. Stakeholders had indicated that obligations for both mandatory routine reporting of sufficiency data (donations, distribution numbers, exchanges between Member States and import/export, clinical use) and for rapid notification in the case of sudden drops in supply, would positively impact on the information available to policy makers and on transparency for citizens. However, they also considered that it would result in significant additional costs and administrative burden for blood and tissue establishments and for authorities. A majority had also considered that mandatory emergency plan requirements would bring some or many improvements towards ensuring sufficiency during crises. Improved inter-Member State trust and BTC exchange (with digital tool support), more appropriate clinical use, reduced wastage, donation promotion campaigns and economic investment were all seen by stakeholders as actions that would support achieving sufficiency of supply.

3 ACTIVITY DATA MONITORING AS A TOOL TO SUPPORT POLICIES FOR SUFFICIENCY – JO WIERSUM

The Dutch vigilance organisation, TRIP, had been contracted by DG Santé to carry out certain technical tasks during 2021, mostly related to leading the work of the SoHO Vigilance Expert Sub-group. The contract had also included a task to propose a minimum data set for blood and blood component activity data that might be mandated for reporting in future legislation. Their expert had consulted EDQM, EMA and key stakeholder organisations to develop proposals that were presented at this hearing.

The expert explained that the collection of blood and plasma data should happen in such a way that different players, professionals, authorities, the European Commission, could use the same source of data for the minimum data set for blood and blood activity. She discussed the need for a core data set that should provide transparency for citizens, information for national

policy makers and vigilance denominators for regulators. Various exercises have taken place in the past with different data sets and varying degrees of completeness. What would be most novel in the new approach would be the reporting of information on cross border distribution and on imports and exports. The expert had worked with stakeholders, including blood establishments, authorities to develop proposals for a minimal annual data set feasible to be reported by blood establishments and hospital blood banks to authorities, and by the authorities to the European Commission. A draft dataset was circulated to stakeholders, with questions, during April 2021 and comments were gathered. A series of challenges were identified relating to definitions and units that would be common to all and to capturing the plasma supply and demand data. While the minimum annual data set appears for feasible blood establishments, monitoring self-sufficiency for plasma for medicinal product manufacture is challenging, given the global nature of the final product supply. It was suggested that an additional dataset should be considered for BE resilience monitoring and to support sharing of components in emergency situations. Proposals for a data set that could be referenced in legislation would be submitted to DG SANTE in June 2021.

An EMA representative noted that during the Covid-19 pandemic EMA had worked with the plasma derived medicinal product (PDMP) manufacturers to monitor the supply situation and this had been very helpful. This experience would be useful going forward.

In an online poll of meeting participants, a majority fully or partially agreed that the proposed data set was feasible to mandate. A significant number indicated that more discussion on the details of the data set was needed. The participants indicated that the biggest challenge would be harmonisation of terminology, obtaining data from hospitals and the administrative burden associated with this reporting obligation.

4 THE RECOMMENDATIONS FROM THE EDQM PLASMA SUPPLY WORKSHOP IN 2019 – FOCUS ON LEGISLATIVE RECOMMENDATIONS - EDQM

EDQM introduced a number of recommendations to that had been agreed at a symposium on plasma supply organised in 2019. The recommendations addressed to the European Commission concerned donor vigilance, plasma collection support to achieve strategic independence of plasma in Europe and an improved legal framework to protect plasma donors. There were also recommendations to Member States, or their competent authorities, on improving plasma collection for a sustainable PDMP availability and on donor vigilance.

There was some discussion on the achievement of strategic independence of plasma supply in Europe, in the context of a global supply chain. The patient organisation, EPODIN, commented that the recommendations clearly set out the ambition of EU independence, particularly from the USA, and from uncontrolled globalisation.

In an online poll of participants, a significant majority fully or partially agreed that revised EU legislation should enhance/enable/safeguard strategic independence in PDMPs. A significant majority also fully or partially agreed that future EU legislation should ensure equitable access to treatment for PDMP-dependent patients although a significant number considered that this needed further discussion. A similar response was seen regarding an evaluation of how the plasma master file process might be adapted to increase the availability of plasma for PDMP manufacture.

5 EUROPEAN BLOOD ALLIANCE – HOW EU LEGISLATION COULD SUPPORT A SUSTAINABLE SUPPLY OF BLOOD AND BLOOD COMPONENTS IN THE EU – CONTINUOUSLY AND IN TIMES OF CRISIS

EBA presented their key recommendations. They stressed that donor bases must be broad to ensure more a more robust supply, without reliance on a small number of frequent donors. A key recommendation from EBA was that Member States should develop national supply monitoring mechanisms, with obligations to share data with EU agencies or the Commission. Their recommendations were summarised as follows:

1. The EU legislation should call for a national self-sufficiency of labile products and for a European strategic independence for PDMPs

2. The EU legislation should set European strategic objectives for European strategic independence in PDMPs

3. European law should call for national strategic plan for sufficiency of BTC that should include strategic objectives proportionate to the MS needs.

4. The EU should encourage and support the development of efficient plasmapheresis collection programmes, based on voluntary non-remunerated donors in the EU Member States.

5. Member States must ensure that all establishments authorised to collect BTC within their territory have access to the donation history of every donor regardless of where their previous donations where performed.

6. European law should oblige MS to share their data, collected from all BTC collectors regularly, with EU agencies and EU institutions.

EBA also highlighted that the supply situation could be improved with certain non-legislative actions. These included training programmes for blood establishments (to help reduce or eliminate the wastage of recovered plasma due to quality concerns); the establishment of transfusion medicine as an independent medical subject with structured training and the implementation of evidence-based usage of immunoglobulins in Member States (Patient IG Management).

An online poll showed positive support among the participants for all of the EBA proposals although a significant number of participants considered that further discussion on details would be needed.

6 EUROPEAN PLASMA ALLIANCE – HOW EU LEGISLATION COULD SUPPORT A SUSTAINABLE SUPPLY OF PLASMA IN THE EU – CONTINUOUSLY AND IN TIMES OF CRISIS

EPA illustrated the need for the EU to collect more plasma, as plasma collection in the EU is not keeping pace with patient needs. EPA said EU patients that are left untreated makes it difficult to resolve the issue within the EU alone. Twenty five per cent of the plasma needed for the EU must be sourced from the US (this is lower than previously reported as it excludes UK). The Covid-19 pandemic has exacerbated the problem. They noted an annual growth >7% of immunoglobulin usage in the EU over recent years and large differences in IG usage

between EU countries and a marked difference between countries in the East and West of Europe. They showed data demonstrating that those (4) Member States where plasma collection is organised in partnership with the private sector do collect more than is needed by their population, while a selection of those that limit collection to the public sector have significant shortfall. On this basis, they promote coexistence and collaboration of private & public sectors to collect more plasma in Europe. They presented three key recommendations.

1. Define and differentiate plasma from whole blood in EU legislation. This should include:

   - Definitions: "plasma for transfusion", "plasma for manufacturing/for fractionation", "recovered plasma", "plasmapheresis", "Blood Establishments" (as proposed by EMA);
   - Inspections: include remote inspections, as well as control measures and introduction of an (EMA backed) risk-based approach as to frequency/intervals of inspections;
   - Revise donor deferral criteria, based on the latest scientific evidence;
   - Cross-reference "plasma for manufacturing" to the EU Medicinal Products Directive and, in the pharma legislation, introduce amendments to trigger the extension of the EU-US Mutual Recognition Agreements to also cover medicinal products derived from human blood or human plasma.

2. Clarify in EU legislation:

   - the role of "health professionals" in plasma centres, without a requirement for a physician presence at all time;
   - that "compensating donors for expenses and inconvenience" is acceptable as compliant with the VUD principle (as in 2004/23/EC, the Council of Europe DH-Bio Committee Guide for the implementation of the principle of prohibition of financial gain with respect to the human body and its parts from living or deceased donors, the German Transfusion Law and a KCE report on "How to ensure self-sufficiency for PDMPs in Belgium").

3. Recommend in EU legislation increased plasma collection to reduce dependency on third countries, the need for plasma awareness campaigns and more plasmapheresis.

An online poll showed significant support for many of the proposals. Almost half the participants (48%) agreed, or partially agreed, that future EU legislation should define and differentiate plasma from whole blood, while the remainder disagreed or considered that more information/discussion on this is needed. Many participants (41%) disagreed that future legislation should recommend a plasma collection model in which the public and private sector operate in coexistence, while significant minorities agreed or partially agreed or considered that more discussion is necessary on the proposal.

7 EMERGENCY/CONTINGENCY SUPPLY (BSCEP) – EDQM

EDQM presented a project they are co-ordinating that is co-funded by the EDQM in the context of a Grant Agreement with the European Commission (2018 53 01). The key objective is to develop recommendations on Emergency Preparedness and Contingency

Planning as a key component National Blood Systems. An ad-hoc working group has been established that has conducted a survey, mapping interventions/tasks implemented by authorities and services at national level. The group will produce a report and recommendations addressing key risk scenarios and presenting actions for different actors including the possible roles of authorities in inspection and authorization, and development of plans. The recommendations will include the cross-country dimension and the need for collaboration and harmonisation. The recommendations will be an input for consideration in the revised BTC legislation and in future Council of Europe standards.

The survey had closed on the 11 March with 31 responses, mostly from national blood services and blood competent authorities and representing 27 European countries. EDQM presented the results of the survey, focusing on those questions that addressed legislation or guidance. Almost 60% of respondents indicated that there is legislation/legislative provisions in place related to emergency preparedness and contingency planning to ensure the continuity of blood supply. A series of specific questions and responses were presented demonstrating a number of aspects that could be considered for inclusion as requirements in future EU legislation. DG Santé confirmed that the final report and recommendations would be a key input in the BTC Impact Assessment.

An online poll showed almost full support for future EU legislation obliging Member States have emergency preparedness and contingency plans in place to ensure continuity of the blood supply. There was considerable support for regulatory authorities being made responsible for inspection and authorization, as well as the development of, contingency plans although participants indicated that more discussion on the details would be needed.

8 THE PATIENT'S PERSPECTIVE ON HOW TO ENSURE A SUSTAINABLE SUPPLY OF PLASMA FOR THE MANUFACTURE OF PLASMA-DERIVED MEDICINAL PRODUCTS.

Two patient representative organisations presented their views on how the EU can ensure a sustainable supply of blood components for transfusion and for the manufacture of PDMPs. Their key recommendations were the following:

PLUS (the Platform of Plasma Protein Users) presented also on behalf of IPOPI (the International Patients Organisation for Primary Immune Deficiencies) and the EHC (European Haemophilia Consortium)

1. A more comprehensive list of more accurate definitions to remove any ambiguities and ensure that the differences between blood and plasma, and their derivatives are better identified
2. Plasma collected solely for the production of medicinal products should be explicitly excluded from the definition of "blood component"
3. Proposed new terms under definitions: Plasma, Plasma for Transfusion, Plasma for Fractionation, Recovered Plasma and Apheresis (Source) Plasma
4. PDMPs are medicinal products that should circulate freely in order to reach patients in need
5. The process for updating BTC technical rules has to involve formal consultation with experts and relevant patient organisations throughout the process. Otherwise, they would be seen as unacceptable and would be of little value to patients.
6. There is not enough plasma collected in the EU. Faced by this challenge, the EU should look at best practice and learn from those countries that are collecting the

highest volumes of plasma in the EU. Adapting these models to the national situation in additional member states will allow an increase in collection.
7. The ultimate goal should not be European sufficiency but global sufficiency based on more regionally balanced plasma collection. Need to place future EU legislation in the international context
8. The new BTC legislation should contribute towards increased supply and free movement of safe and efficacious PDMPs
9. Avoid wastage and encourage plasmapheresis whenever possible

EPODIN (European patients living with inflammatory and dysimmune neuropathies) recommended that the future EU legislation should:

1. Protect donors (number of donation per year and donor monitoring tools)
2. Maintain the principle of free donation but leave open the possibility of offering compensation as long as this does not constitute a form of salary, which is in line with the protection of donor (number of annual donations and strict monitoring)
3. Give priority to the country of origin of the plasma collection (and in any cases to the EU)
4. Allow a cohabitation of public-private collection systems under the responsibility of the member states under the authority of the EU legislation within strict limits of donor protection with (accessible) tools for full traceability
5. Encourage its implementation in the health systems of the Member States.
6. Integrate ethical issues into the guidelines (considering, for example, whether plasma collected with a regulation that allows 104 donations per year (US) and a regulation that allows 33 (most of the EU) should be evaluated in the same way in the Plasma Master File.

9 THE DONOR PERSPECTIVE ON HOW TO ENSURE A SUSTAINABLE SUPPLY OF BLOOD AND BLOOD COMPONENTS – INTERNATIONAL FEDERATION OF BLOOD DONOR ORGANISATIONS

The International Federation of Blood Donor Organisations presented its recommendations on achieving blood and blood component sufficiency as follows.

1. To build and maintain a population of healthy and loyal blood and plasma donors, support and funding from health authorities is required.
2. Blood legislation should include a national blood system and nationally recognized blood donor organizations should be promoted and adequately supported and based on the principle of voluntary unpaid donation (VNRBD). The safety of VUD donations is high because they are regular donors, familiar with the rules for donation and well known to their blood centres.
3. VNRBD is in in the interest of Public Health and must not be jeopardised.
4. National self-sufficiency plans for blood and blood components, including plasma for fractionation, should be systematically in place, to secure availability of needed medicines and avoid shortage.
5. Such plans should be pursued sharing strategic goals with blood donor organizations and protecting the health and rights of whole blood and apheresis donors.

6. Up-to-date principles of social marketing should be applied to recruitment, retention and education of blood and plasma donors if a secure and safe blood and plasma supply is to be ensured, especially in case of exceptional events.
7. It is fundamental for any well performing national blood system to establish a long-lasting relationship with donors and their social environment, since this can enhance safety, consistency and flexibility of supply, cost-effectiveness and blood safety.
8. There is evidence that blood donor organizations and associations can represent a very valuable resource for national blood systems, contributing to the establishment of appropriate social marketing policies within which they can play a strategic role in enhancing the efficiency, cost-effectiveness and sustainability of national and domestic blood systems. Even more so in times of crisis.

10 WORKSHOP CLOSE

DG Santé thanked all participants for the rich discussions and clear positions presented. It was noted that there would be opportunities for further discussion on the VUD topic during a subsequent workshop on Ethical issues. The information provided and views expressed in this and all other workshops will feed into the Impact Assessment process.