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To:

- Peter Richardson, BWP Scientific Secretariat Chair, EMA
- Caroline Voltz-Girolt, BPWP Scientific Secretariat and EMA Product Lead (EPL)

Cc:

- Guy Rautmann, Department of Biological Standardisation, OMCL Network & HealthCare (DBO), European Directorate for the Quality of Medicines & HealthCare (EDQM), Council of Europe;
- Stefaan Van der Spiegel, Head of Sector, European Commission, DG SANTE, Dir. B4;
- Deidre Fehily, Policy officer, European Commission, DG SANTE, Dir. B4;
- Sylvain Giraud, Head of Unit, European Commission DG Sante, Dir. B4;
- Silvia Domingo-Roige, Quality of Medicines, EMA

15 September, 2020

Proposals for revision of donor deferral criteria in the context of the COVID-19 situation in order to maintain access to plasma-derived medicinal products for patients in EU

Dear Dr. Volt-Girolt,
Dear Dr. Richardson,

IPFA and PPTA would like to follow-up with you on our recent requests to the European Commission (EC) for short- and mid-term actions to increase the amount of plasma for manufacturing. The COVID-19 pandemic had and continues to have multiple impacts on plasma and plasma-derived medicinal products (PDMPs) operations and supply. A decrease of the annual projection of the European collection of plasmapheresis plasma for fractionation by the private sector is foreseen as plasma donations declined significantly for a couple of months during the first wave of the COVID-19 pandemic in the U.S[1] and in Europe. Because of social distancing and other measures put in place to mitigate the spread of the novel coronavirus, donor availability and accessibility was limited. This will reflect on Immunoglobulin and other PDMPs availability.

[1] The Wall Street Journal. Coronavirus Pandemic Slashes Donations of Lifesaving Plasma. 19 August 2020. https://www.wsj.com/articles/coronavirus-pandemic-slashes-donations-of-lifesaving-plasma-11597828589

IPFA and PPTA have been made aware that EMA is currently conducting an assessment on the European Union (EU) donor deferral criteria as per the Annex III[2] of 2004/33/EC and EDQM Guide to the preparation, use and quality assurance of blood components ('The EDQM Blood Guide')[3].
In view of this assessment, IPFA and PPTA would like to highlight a number of important donor deferral criteria, which would benefit from re-evaluation, based on current scientific developments and manufacturing processes. Re-assessment of these criteria would increase the amount of plasma for fractionation and availability of PDMPs, without negatively impacting the safety margin of these products. IPFA and PPTA consider this particularly important due to the global and ongoing impact of the COVID-19 pandemic: Some companies are currently experiencing a range of impacts on their activities in Europe, which may, in the long-term negatively impact their ability to provide PDMPs to patients in the EU.

The EMA/ EC adaptation to the regulatory framework to address challenges arising from the COVID-19 pandemic for pharmaceutical companies has been welcomed by our members. IPFA and PPTA kindly requested short term and mid-term actions at EU level, i.e. adjustments and regulatory flexibility with regards to inspections modality in the absence of traveling. IPFA and PPTA are very pleased with the introduction of remote GMP inspections and risk-based approach of plasma centres as well as other regulatory flexibility measures, in line with our recommendations.[4]

To maintain sufficient levels of plasma for fractionation and access to PDMPs for European patients IPFA and PPTA are of the opinion that additional measures should be taken, based on scientific evidence and rationale, as for instance those implemented in April by the U.S FDA with regard to donor deferral criteria for plasma donors. Furthermore, we are of the opinion that alignment of EU and U.S donor eligibility requirements should be sought, where possible, bearing in mind that currently 37% of plasma for fractionation used to manufacture PDMPs for patients in Europe is collected in U.S plasma centres.

Please see below our detailed proposals for changes to the donor acceptance criteria, with regard to plasma for fractionation.

1. Donor deferral based on exposure/ risk of acquiring a transfusion-transmissible infection

1.1 Risk classes and groups:

a. Sexual behaviour, (i.e. MSM, sexual contacts with individuals with HIV risk behaviour):

Change from permanent to 2- or 3-month temporary deferral for a history in the past 2 or 3 months for sexual behaviour (i.e. MSM, sexual contacts with individuals with HIV risk behaviour). The U.S FDA adopted a 3-month deferral for most of the criteria listed[5].
Whilst we appreciate that sexual behaviour and risk assessment for MSM in particular falls under individual EU Member State remit, we would welcome a clarification from a regulatory point. The issue of divergent MSM deferral times (see attached table) in the EU has been reiterated during past IPFA/PPTA/EMA BWP and BPWP Secretariat annual face-face meetings and the need for a position from EMA stating that the quality and safety of the PDMPs remain the same regardless of the

[2] COMMISSION DIRECTIVE 2004/33/EC of 22 March 2004 implementing Directive 2002/98/EC of the European Parliament and of the Council as regards certain technical requirements for blood and blood components; https://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2004:091:0025:0039:EN:PDF.
[3] 20th Edition of the Guide to the preparation, use and quality assurance of blood components. European Committee on Blood Transfusion (CD-P-TS). https://www.edqm.eu/en/blood-guide
[4] NOTICE TO STAKEHOLDERS QUESTIONS AND ANSWERS ON REGULATORY EXPECTATIONS FOR MEDICINAL PRODUCTSFOR HUMAN USE DURING THE COVID-19 PANDEMIC. Revision 3 – 1 July 2020. https://ec.europa.eu/health/sites/health/files/human-use/docs/guidance_regulatory_covid19_en.pdf
[5] Revised Recommendations for Reducing the Risk of Human Immunodeficiency Virus Transmission by Blood and Blood Products. Guidance for Industry. AUGUST 2020. https://www.fda.gov/regulatory-information/search-fda-guidance-documents/revised-recommendations-reducing-risk-human-immunodeficiency-virus-transmission-blood-and-blood

national recommendations for donor acceptance, was repeatedly requested and is also supported by the Platform of Plasma Protein users (PLUS). We are aware that EMA is currently working on that topic and a discussion with the EC is ongoing.

b. Tattoos, piercings, and needle sticks:

We would recommend reducing the deferral from 6 months to 2 or 3 months for tattoos and piercings and put in place a no deferral for procedures which are carried out in health care regulated establishments and with single-use needles. Donor motivation surveys as well as published literature[6] show that even a temporary deferral of existing donors due to tattoos and piercings leads to permanent loss of donors, without resulting in higher transfusion-transmission of infections**.** Currently, Annex III of 2004/33/EC stipulates a 4-month deferral, provided a NAT test for hepatitis C is negative, a 2 or 3 months' deferral should be considered, and no deferral should be put in place when above procedures are performed by a qualified practitioner with sterile single use needles and sterile, single-use equipment/non-reused ink. In addition, no deferral should apply to acupuncture treatment if done under a professional medical practice establishment in a highly regulated environment that requires single use needles.

c. Other:

- Mucosal splash with blood or needle stick injury, as well as transfusion of blood components: Change from 6 month deferral (or 4 months with negative HCV NAT) to a 2 or 3 month deferral for a history in the past 3 months of mucosal splash with blood or needle stick injury, as well as transfusion of blood components.
- HCV: Exposure to persons at risk for HCV or tested positive for HCV: A reduction of deferral period from 4 months to 2 or 3 months upon negative NAT test should be considered.

2. Donor deferral based on other criteria

2.1. Haemoglobin measurement[7]:

For plasma for fractionation, the measurement of haemoglobin levels should be replaced for by a relevant parameter, such as IgG.

2.2. History of malignant disease:

Basal and squamous cell melanomas should be excluded.

2.3. Endoscopic procedures:

Deferral should be removed, as risk of transfusion-transmissible infection is already covered by Annex III in the "transfusion of blood components" category.

2.4. Pregnancy:

Deferral should be reduced to 6 weeks after delivery or termination, unless breastfeeding, in which case, deferral until breastfeeding is discontinued.

The comments on the need for re-evaluation of donor deferral criteria based on scientific evidence were submitted by IPFA and PPTA during the public consultation on the 20th Edition of the Blood Guide, but were not implemented. They also were proposed independently by IPFA and PPTA during the assessment of the European directives on Substances of Human Origin (SoHO) by the European Commission in 2019.

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[6] No increased risk of transfusion-transmissible infections after tattooing, body piercing, or acupuncture among blood donors in the Netherlands: Femmeke J. et al; Transfusion, Volume 59, Issue 8, August 2019. https://onlinelibrary.wiley.com/doi/10.1111/trf.15421

[7] Frequent source plasma donors are not at risk of iron depletion: the Ferritin Levels in Plasma Donor (FLIPD) study: Schreiber GB. Et al; Transfusion, Volume 58, Issue 4, April 2018. https://onlinelibrary.wiley.com/doi/abs/10.1111/trf.14489

Conclusions:
The impact of COVID-19 on our members is substantial and poses long-term challenges in addressing the urgent need for plasma for manufacturing of PDMPs in Europe. IPFA and PPTA consider these changes are science-based and would allow maintaining highest standards of safety for donors and recipients. We would like to reiterate that the suggested changes to donor deferral criteria would assist our members to supply safe and effective essential PDMPs during the COVID-19 pandemic to European patients.

Translation of any revision to criteria into the Blood Guide by the EDQM CD-PTS and associated Directives[2] would need consideration in due time.

IPFA and PPTA would also like to take this opportunity to recommend as a best practice the participation of PDMP manufacturers' Associations at dedicated BWP Working Group meetings related to revision on donor deferral criteria.

IPFA and PPTA remain at your disposal for any questions you might have.

With kind regards,

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IPFA

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PPTA