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EUROPEAN COMMISSION
DIRECTORATE-GENERAL FOR HEALTH AND FOOD SAFETY

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

Competent Authorities of Substances of Human Origin Expert Group (CASoHO E01718)

Meeting of the Competent Authorities for Blood and Blood Components

18-19 February 2020

Summary Minutes

The meeting of the Competent Authorities for blood and blood components (CAs) took place on the 18-19 February 2020. The previous meeting had taken place on 18-19 June 2019.

PARTICIPATION

CAs from all Member States (MS) attended the meeting, except for Latvia, Slovenia and Luxembourg. In addition, CAs from Norway, Turkey, Montenegro and the Republic of North Macedonia were present. Furthermore, the meeting was attended by representatives from the European Centre for Disease Prevention and Control (ECDC), the European Medicines Agency (EMA), the Council of Europe (EDQM) and the World Health Organisation (WHO). Representatives of the TRANSPOSE project and rapporteurs of the Vigilance Expert Sub-Group and of the Inspection Expert Sub-Group also attended.

The representatives of the European Commission/DG SANTE unit B4 chaired the meeting.

1. WELCOME AND INTRODUCTORY REMARKS

The chair welcomed the participants and asked representatives attending for the first time to present themselves. Following this, the SoHO team members introduced themselves to the new representatives and they informed the attendees about the usual house rules.

2. ADOPTION OF THE AGENDA

No additional topics were added to the agenda. Participants were invited to state any conflicts of interest. No conflicts of interest were declared.

3. REGULATORY MATTERS: POINTS FOR INFORMATION

3.1. Transposition, complaints, court cases and parliamentary questions

At the end of 2019, DG SANTE completed the conformity check for the transposition of Directive (EU) 2016/1214 (amendment of Directive 2005/62/EC to reflect the development of the GPG). As of February 2020, transposition is considered adequate and complete in all MS except for one, which still requires further follow-up.

DG SANTE informed the participants that of the two complaints against MS in the areas of plasma procurement and contract manufacturing, one is to be closed, since the MS has notified amendments to national legislation, and the second one is still open (letter of formal notice) and is followed up by DG GROW. There are on-going complaints against three MS regarding the deferral of men having sex with men (MSM).

3.2. Update by the Netherlands on deferral after tattoos, piercings and acupuncture

NL gave an update to the participants on possible changes in the deferral policy for donors after recent tattoos, piercings or acupuncture. NL presented the results of a study that revealed no increased risk for transfusion transmissible infections and questioned the current deferral period of 4 months for donors following tattooing, piercing or acupuncture in a Dutch establishment. NL emphasised the importance of a revision of the BTC legal framework that will enable them to implement this policy change.

EDQM suggested that this information should be channelled into the work for the next version of the blood guide that will start in April, as it can also be valuable for other countries.

FR will conduct a re-evaluation of all donor deferral criteria in two years, where this issue will also be considered.

3.3. Other Member State legislative updates

DK reported to have implemented a change in the deferral time for MSM. As of 22 March 2020, MSM donors will only be deferred for a period of 4 months since the last sexual contact. DK will also accept donations of plasma for fractionation from this group.

All MS were asked to notify the Commission if they consider changing their MSM deferral policies.

EDQM stated that they have conducted a survey in all member states of the Council of Europe (CoE), where different MSM deferral policies were reported. The results will be provided to the Commission for sharing with the CAs. It was reported that the plasma industry does not accept plasma for fractionation from MSM donors. Hence, there might be problems with DK's new policy and the question was raised whether plasma derived medicinal products (PDMP) from DK's plasma will all go back to DK.

FR and FI reported that they are also considering changing the deferral period for MSM donors.

EMA was asked whether it was ready to make a statement about an acceptable MSM deferral period for plasma for fractionation. The representative stated that it is not possible for them in the current organisational situation, as they are just taking up full activities again after the recent move of headquarters. They will consider this issue as soon as possible.

4. FOLLOW-UP TO THE EVALUATION OF THE BLOOD LEGISLATION

4.1 Key messages of the Evaluation

DG SANTE summarised the findings of the Blood, Tissues and Cells Evaluation (BTC Evaluation), which was completed in October 2019.

The BTC Evaluation revealed that EU legislation has effectively helped increase the safety and quality of blood, tissue and cell therapies. However, five key challenges were identified that require further action:

1. Keeping legislation up-to-date in a dynamic sector with changing risks
2. Ensuring that all EU citizens affected by the BTC chain are protected
3. Providing appropriate and robust oversight
4. Keeping pace with innovation in BTC for patient benefit
5. Achieving sufficiency and a sustainable supply to meet patient need

The next steps for the Commission are to disseminate the findings of the BTC Evaluation and to draft an Inception Impact Assessment (IIA) defining some broad policy options, which will be published for a feedback period. The IIA will be followed by a full Impact Assessment of the selected policy options. The process will involve stakeholder consultation and an external study. Follow-up initiatives will be taken forward based on the results of the Impact Assessment.

DK and PL both raised calls for an urgent revision of the BTC legislation.

The Commission thanked all CAs for their engagement in the evaluation process and asked them to provide feedback on the IIA once it is published.

4.2 Debrief of meetings with stakeholders

The Commission provided information on recent meetings with stakeholders from the plasma sector. In December 2019 and January 2020, the Commission had met with representatives of the public plasma sector, the plasma and blood bag industries and patient organisations. Specifically, there were meetings with the International Plasma and Fractionation Association (IPFA), the Plasma Protein Therapeutics Association (PPTA), the European Blood Alliance (EBA), the Blood Transfusion Association (BTA), and the European Patient Organisation for Dysimmune and Inflammatory Neuropathies (EPODIN).

DK, SK and CZ emphasised the importance of voluntary unpaid donation (VUD). They argued that paid donations might lead to a decrease in the quality and safety of substances and underlined that it is indeed possible to increase the plasma supply through VUD.

5. INSPECTION AND AUTHORISATION

5.1 Update from the Inspection Expert Sub-group (IES)

A representative of the IES presented the progress made with the 2019 IES Work Plan. The Work Plan consists of five Work Clusters, focusing on (1) reviewing and developing guidance documents, (2) coordination of inspector training courses, (3) oversight of joint/observed inspections, (4) oversight of inspection system audits, and (5) dissemination and monitoring of the results. Progress has been made in all five Work Clusters, but there are still on-going activities and pending decisions.

The next steps include finalising the 2019 Annual Report and preparing the 2020 Work Plan. Having developed a clear set of priorities and working methods, the sub-group now aims to move to a more operational phase in 2020. The subsequent IES meeting was held on 20 February 2020 one day after the CA meeting.

A representative of the IES also presented the results of a survey of CAs on joint inspections, which demonstrated that many CAs already have some experience with joint inspections and that there is an overall high interest in hosting and joining joint inspections.

The attendees of the meeting expressed appreciation for the work of the IES and welcomed the progress that has been made.

5.2. Other Member State updates on inspections

The chair of the meeting asked the CAs if they had any national developments related to inspections that they would like to inform the other CAs about. No updates were given.

5.3. Update on the GAPP Joint Action on preparation process authorisation

The EU funded Joint Action facilitatinG the Authorization of Preparation Processes for blood, tissues and cells (GAPP) aims to support the development of a common and optimal approach to assess and authorise preparation processes in blood, tissue and cell establishments. The Joint Action has 24 beneficiaries (CAs, scientific societies, blood and tissue establishments, hospitals etc.) from 17 countries. It started in May 2018 and runs for 3 years.

The CAs received an update on the progress made in the different Work Packages. One particular aspect that GAPP is working on is the assessment of clinical outcome/efficacy of blood therapies in addition to existing quality and safety requirements for the authorisation of novel preparation processes.

The participants of the meeting welcomed the progress of the GAPP Joint Action and expressed appreciation for their work.

5.4 Inspections of plasma collection centres in third countries

EMA provided information on inspections of plasma collection establishments in the US that they co-ordinate with national pharmaceutical authorities, on a risk-based frequency. This system is separate from the inspections of fractionation sites under the agreements on Good Manufacturing Practice (GMP). Past inspections have revealed that there is high compliance of US plasma establishments with the EU standards and EMA agreed to make the reports of inspections available to the CAs through DG Santé. The Food and Drug Agency (FDA) in the US has asked if there is a possibility to recognise the inspections performed by them and thus eliminate the necessity of inspections by EMA in the US. This would require auditing the FDA blood inspection system. So far, no decision has been taken on this matter.

6. VIGILANCE AND SURVEILLANCE

6.1. ECDC update

ECDC informed the group regarding recent infectious disease outbreaks that pose potential threats for blood transfusion.

The main topic was the current outbreak of the SARS-CoV-2 virus that causes the disease COVID 19. The risk of transmission through SoHO is unknown and ECDC assumes that routine donor screening measures should already prevent individuals with clinically manifest respiratory infections from donating SoHO. Nevertheless, ECDC recommends some additional precautionary measures for blood establishments that have already been communicated to CAs

and implemented in blood establishments. The ECDC representative also gave a short update on the outbreak of the Ebola virus disease in DRC and Uganda since 2018, which currently sees a decline in the numbers of new cases.

Furthermore, the event and threat management solution (ETMS) was introduced, which replaces the existing Epidemic Intelligence Information Systems and the ECDC Threat Tracking Tool and enables experts to exchange technical information on current and emerging public health threats. At least one representative from CAs and one from SoHO national services should participate in this initiative.

ECDC informed the participants that they are hosting a Notify library editorial board meeting on 5-6 May 2020.

6.2. Rapid alerts - General overview

DG SANTE provided the participants with a summary of alerts posted in the RAB platform up to February 2020. There is no observable trend in the number of RABs reported between 2013 and 2019. A total number of 21 alerts (epidemiological alerts, Quality and Safety defects and information notices,) had been reported via the platform in 2019. So far, no CAs have reported RABs in 2020.

6.3 Member State surveillance updates

EL provided information on an international collaborative workshop on the contribution of haemovigilance in relation to infectious risks of transfusion and malaria specific interventions that will be held on 18-19 March 2020 in Athens.

6.4 SARE reporting

The Council of Europe (EDQM) debriefed the participants on the analysis of the 2019 Serious Adverse Reactions and Events (SARE) reporting exercise for Blood (2018 data). EDQM noted that there is a gradual improvement in data collection, but that also SARE data are still missing from two MS and that some MS do not report all denominators. In addition, EDQM observes inconsistency and heterogeneity between the MS in their reporting activities.

In April 2020, the Commission will launch the 2020 SARE reporting exercise with a deadline in July 2020. There will be some changes in the reporting template and some clarifications in the Common Approach document. EDQM asked all CAs to read the Common Approach carefully to improve the consistency of reporting.

CAs suggested some improvements to SARE data collection, such as investigating long-term consequences and statistical significance of findings. CZ noted that they have difficulties with data collection and that it is challenging to ensure that all physicians use the Common Approach. This might be further complicated if the Common Approach is updated frequently. EDQM stated that they are aware of these challenges and that they are planning to organise a vigilance training to achieve more consistent data collection.

The Commission thanked EDQM for their efficient and dedicated work in this data collection exercise.

6.5. Feedback from Vigilance Expert Sub-group (VES)

The Vigilance Expert Sub-group's (VES) is a sub-group to the expert group CASoHO E01718, working on vigilance across blood, tissues and cells with the aim of improving the Commission's vigilance related activities, particularly the SARE and rapid alerts programmes.

The VES rapporteur provided an update of the work of the sub-group. VES received a new wave of proposals for improvement of vigilance in 2018/2019. The proposals most relevant to the blood sector were to improve the severity assessment of SAR by providing clear definitions for the different levels of seriousness, and to provide clearer and further categories for SAE reporting. For this purpose, the new category of "system failure" has been created and the category "human error" has been divided into two sub-categories: "incorrect decision or omission following the correct procedure" and "following the wrong procedure".

DG SANTE supported this initiative and thanked the VES for their work.

7. BLOOD SERVICE RE-ORGANISATION – ROMANIA AND HUNGARY

RO and HU gave an introduction of their respective health systems and blood sectors. RO is currently implementing a Plan for Action for the reorganisation of the blood collection and transfusion system and the design of an appropriate oversight system that has been approved for financing through the Structural Reform Support Program 2017-2020 (DG REFORM). HU presented their problems and plans with regard to human resources in the blood sector.

The representative of DG REFORM introduced the activities of the DG in providing support to MS that are carrying out structural reforms. MS who wish to receive support from DG REFORM should submit their official requests by 31 October. MS that consider reforms are welcome to contact DG REFORM in order to receive support in the formulation of requests. All requests must, however, be submitted firstly to the national co-ordinator for the programme (the contact details in MS were provided in a previous meeting).

8. DEVICES AND DIAGNOSTICS

8.1 Impact of DEHP ban on the supply of blood bags

The Commission provided an update on the impact of the inclusion of DEHP on the REACH list, which implies a ban on its use in medical devices. Currently, there are alternatives to DEHP for blood bags that are used for components other than red blood cells. For these components, the medical device industry is urged to proceed to non-DEHP products without delay. For red blood cells, where DEHP has a beneficial effect on the preservation of the cells, the medical device industry should continue to explore alternatives to DEHP and where necessary, apply to REACH for approval to continue the usage of DEHP-containing bags. CAs are advised to follow the progress of this topic with their BEs to ensure that appropriate measures are taken to avoid sudden interruptions to supply.

8.2 Classification of blood bags

Representatives of the medical devices unit DG SANTE B6 (formerly DG GROW D4) provided information on the up-classification of blood bags under the new Medical Devices Regulation (MDR). In the MDR, all medical devices that contain a medicinal product will be classified as class III, which also applies to blood bags containing anticoagulants and other solutions. Under the current directive, blood bags are classified as class IIb, unless they have a function beyond storage. For class III medical devices, a clinical evaluation is necessary to prove conformity with relevant safety and performance requirements, which is to be repeated

in case of device changes. The manufacturer is responsible for deciding which data are needed for the clinical evaluation and B6 is currently developing guidance on clinical evidence that is required for legacy devices, such as blood bags that are already on the market.

When asked about the reasons for the up-classification of blood bags, the B6 representatives explained that the new rule does not apply only to blood bags, but to a much larger range of devices.

8.3 Borderline group with Medical devices

There is a new task force in the medical device Borderline and Classification Working Group (BWCG), where tissue and cell CA representatives will join medical device CAs to address borderline issues. This task force is developing guidance with respect to the scope of the MDR when devices contain human tissues and cells or their derivatives, and on the procedure for consultation with tissue and cell CAs, as required by the legislation for those products where tissues and cells have an ancillary action to the device. Tissues and cells authorities had been invited to prepare proposals for how the consultation procedure should work.

It was suggested that the CD-P-TS could also be involved in the discussions about borderline cases.

9. CONTINUITY OF SUPPLY AND EMERGENCY PLANNING

EDQM introduced the work of TS093 on Plasma Supply Management, an expert group which started its work in 2013. In the context of the grant agreement with the Commission, the group organised a symposium in January 2019, in which recommendations for ensuring the continuity of plasma supply were developed. These recommendations include, among others, increasing awareness of the need for increased plasma collection, providing adequate funding to blood establishments, designing national programmes targeting plasma needs, monitoring the PDMP inventory of companies, providing reports on annual plasma collection and PDMP use, monitoring off-label and inappropriate PDMP use, developing contingency plans, enforcing donor vigilance and considering an international harmonised approach for the qualification of staff in blood establishments.

10. COUNCIL OF EUROPE UPDATE

EDQM presented the activities of the European Committee (Partial Agreement) on Blood Transfusion (CD-P-TS). Besides the project on plasma supply management, they are currently working on a project on risky donor behaviour and the safety of transfusion, as well as on the 20th edition of the blood guide. The Commission will share the final version of the Good Practice Guidelines (GPG) with the CAs.

EDQM also provided an update on other activities included in the grant agreement with the EU for 2019-2021. In this context, EDQM is organising activities in the fields of biovigilance, quality management, country assessment missions in EU candidate, applicant and neighbourhood countries, and continuity of supply and emergency planning.

SK reported that they have difficulties with the legal reference to the GPG, as their national system requires them to go through a lengthy implementation process every time the GPG is updated. Other MS provided some advice on how the 'dynamic reference' could be implemented into national legislation.

11. PRESENTATIONS OF OTHER EU-FUNDED ACTIONS

11.1 TRANSPOSE project

TRANSfusion and transplantation PrOtection and SElection of donors (TRANSPOSE) is a Public Health Programme project aimed at improving donor selection policies and ensuring donor safety in the collection of SoHO for transfusion and transplantation purposes. The initiative started in 2017 and will end in 2020. There are 7 work packages, including 4 technical work packages. There was a workshop for dissemination of the results of the project scheduled for the week subsequent to the CA meeting, i.e. on 24-25 February 2020. The deliverables will be used by EDQM for the development of future versions of the Guides to Quality and Safety of blood and blood components.

The TRANSPOSE representatives presented the results of Work Package 6, which focuses on the development of a standardised donor health questionnaire, and Work Package 5, which focuses on the development of donor selection and protection criteria.

The Commission thanked TRANSPOSE for their dedicated work and stated that the results will be valuable in the follow-up of the BTC evaluation.

12. RESEARCH AND DEVELOPMENT

The Commission provided information on the Horizon Europe programme, which allocates ca. 7.7 billion € to research and innovation in health. The targeted impacts of the health cluster of Horizon Europe were presented and preliminary ideas were exchanged on how these could be linked to the SoHO sector. CAs were encouraged to send further ideas and suggestions to the Commission as a follow-up to the meeting.

13. EMA UPDATE

EMA presented the progress of the Blood Products Working Party (BPWP) in 2018 and provided an update on the current situation of EMA in the light of Brexit. EMA had to leave its premises in London in 2019 and has now moved to its permanent premises in Amsterdam. Non-critical activities that have been placed on hold during the time of the move will be re-initiated, but EMA has to deal with a reduced number of staff. Thus, they will focus on the core activities in defining their work programme for 2020 and prioritise additional activities depending on the available resources. The core activities include Plasma Master File (PMF) certification.

14. WHO UPDATE

WHO provided an update on relevant developments in WHO for the blood and plasma sectors. A new department for Blood and other Medical Products of Human Origin (MPHO) has been created in the WHO headquarters. Furthermore, WHO has launched an Action Framework to advance universal access to safe, effective and quality-assured blood products for the years 2020-2023 and developed a Biennium Work Plan on Blood for 2020-2021.

The Commission thanked the WHO representative for her presentation and suggested that there should be further reflections on how the EU and the WHO can collaborate in the future in the blood and plasma sector.

15. ANY OTHER BUSINESS

No additional points were raised.

16. FINAL REMARKS

The Chair thanked the group for their active participation in the meeting and informed them that the next meeting of the blood CAs is planned for 15-16 October 2020.