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

Meeting of the Competent Authorities for Blood and Blood Components

18-19 June 2019

Summary Minutes

The meeting of the blood and blood components competent authorities took place on the 18-19 June 2019. The previous meeting had taken place on 10-11 October 2018.

PARTICIPATION

Competent Authorities from all Member States (MS) attended the meeting, except for Italy, Hungary and Luxembourg. In addition, competent authorities from Norway and from the Former Yugoslav Republic of Macedonia were present. Representatives from the European Centre for Disease Prevention and Control (ECDC), the Council of Europe (EDQM) and the World Health Organisation (WHO) as well as a rapporteur of the Vigilance Expert Sub-Group also attended. The EMA representative could not attend the meeting.

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 (CY, RO, AT) to present themselves. Following this, the SoHO team members introduced themselves to the new representatives and they informed the meeting about the usual house rules.

2. ADOPTION OF THE AGENDA

No additional topics were added to the agenda although the order was changed for some topics to accommodate the travel plans of particular speakers. Participants were invited to state any conflicts of interest. None was declared.

3. REGULATORY MATTERS: POINTS FOR INFORMATION

3.1. Transposition, complaints, court cases and parliamentary questions

The deadline for transposition of Directive (EU) 2016/1214 (amendment of Directive 2005/62/EC to reflect the development of the GPG) was 15/02/2018. By this deadline, 13 Member States had notified their transposing measures. Letters of Formal Notice were sent to 15 Member States. By 2019, all Member States had notified transposing measures and the infringement proceedings were closed.

In 2018, DG SANTE began the conformity check. DG SANTE considers the transposition in majority of the Member States as adequate and complete. Clarifications were being requested from four Member States. As of June 2019, 5 MS still had to be assessed.

DG SANTE informed the participants that of the three complaints against Member States in the areas of plasma procurement and contract manufacturing, one had been closed with no further action, the second was still open and awaiting amendments to national legislation (following Court ruling) and the third one was open (letter of formal notice). The complaint regarding VUD labelling of PDMPs was ongoing. As these complaints raise concerns about public procurement practices in the Member States, the Commission explained that its Directorate General GROW is leading for these cases with DG SANTE closely associated.

3.2. MSM update from Denmark and Finland

DK gave an update to the representatives on the status of eligibility of men having sex with men (MSM) to donate blood in Denmark and its amended legislation. Currently in DK, MSM are permanently deferred from blood donation. DK noted that the deferral has become temporary in many EU and third countries, usually with a 12 deferral since the last sexual contact. This has been reduced further to three months in the UK. A project plan was developed in summer 2018 to change this rule, allowing a temporary deferral, the period of deferral is under discussion. First updates are expected in 2019-2020, which will lead to the updating of existing national regulations.

BE asked if there are provisions governing blood donation in other MS with regard to transgender. For the moment there are no regulatory provisions in BE. Other MS mentioned that neither in their MS are provisions in place.

FI also presented their discussions on the topic of blood donation by MSM. They have already implemented a temporary deferral (12 months) but discussions continue on further changing this, with an evaluation and stakeholder consultation ongoing.

DE asked if the countries present discard the plasma of MSM donors, noting that the plasma industry does not accept plasma from MSM. DK accepts plasma from MSM after four months from the last sexual contact. CZ accepts but only after 12 months.

3.3. Other Member State legislative updates

UK mentioned the progress with the ongoing inquiry on infected blood in the 1980s and early 1990s. The inquiry examines why men, women and children in the UK received infected blood and infected blood products, the impact on their families, how the authorities responded and the nature of any support provided in cases of infectious transmission etc. The Inquiry has begun its investigative work. The first stage is to obtain evidence and witness statements. More information concerning the ongoing inquiry can be found at https://www.infectedbloodinquiry.org.uk/.

4. EVALUATION OF THE BLOOD LEGISLATION

DG SANTE summarised the state of play of the Blood, Tissues and Cells Evaluation (BTC Evaluation), explaining that the Commission's Evaluation Report was expected to be published in autumn 2019.

The key issues coming forward from the Commission's stakeholder consultation activities, focusing on activities and messages emerging since the previous meeting, were outlined. The key findings emerging out from the evaluation, overall, were the following:

- Technical provisions of the legislation are out-of-date in a rapidly changing sector;
- Oversight provisions are not adequate to regulate today's BTC landscape;
- Some citizens groups are not adequately protected (donors, children born from medically assisted reproduction);
- Innovation in BTC is not optimally facilitated;
- Limited provisions to ensure BTC sufficiency.

These findings come from the Open Public Consultation conducted by the Commission[1], including submissions from a broad spectrum of stakeholders from different sub-sectors from multilateral meetings between stakeholders, the Commission and MS authorities [2] and an external study.

Some NCAs re-emphasised important shortcomings in the BTC legislation such as the borderline product classification issue. NCAs expressed their anticipation of a possible revision of the BTC legislation after the evaluation is completed.

DG SANTE representatives summarised the next steps and the planned timing for publication, noting that it would be up to the new Commission to consider how to address the shortcomings and gaps identified during the process. They thanked Member States for all their contribution to the process so far and urged them to inform DG SANTE if they have any comments regarding the findings outlined to date. In addition, they were invited to submit any additional data/evidence they considered important and encouraged to disseminate the report once published. Outputs are available on the DG SANTE website.[3]

5. INSPECTION AND AUTHORISATION

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

The meeting was given an update on the work of the expert sub-group on inspections (IES) since its establishment in 2018. The representatives were reminded that a proposal to establish such a sub-group was first made in the October 2018 to the CASoHO Expert Group meeting (Competent Authorities). Terms of Reference were then agreed in writing by both the blood and tissues, and cells competent authorities. DG SANTE called for nominations at the end of 2018. 28 competent authorities nominated 45 representatives. The first IES meeting took place in January 2019.

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[1] https://ec.europa.eu/health/blood_tissues_organs/consultations/implementation_legislation_en.
[2] The key messages emerging from those meeting were summarised and the meeting participants were referred to the webpage where summary minutes are published: https://ec.europa.eu/health/blood_tissues_organs/events_en#anchor1.
[3] Summary of the Stakeholder consultation on the BTC Evaluation:
https://ec.europa.eu/health/blood_tissues_organs/consultations/implementation_legislation_en
https://ec.europa.eu/health/sites/health/files/blood_tissues_organs/docs/2018_consultation_evaluationbtc_report_en.pdf.
Summary of the Blood, Tissues and Cells Stakeholder Event of 20/9/2017:
https://ec.europa.eu/health/sites/health/files/blood_tissues_organs/docs/ev_20170920_sr_en.pdf.

The IES involves both blood and tissues and cells CAs, the meetings take place at least twice a year. A first meeting was held in January 2019 and a second took place after this CA meeting (20 June). The work is based on the 2019 Work Plan which was endorsed by blood and tissues and cells CAs by written procedure on 24 May. The IES focus its work on the following areas:

(i) review of existing guidance documents on inspections and inspections systems and the development of new guidance documents;

(ii) development and coordination of training courses on inspection and the audit of inspection systems;

(iii) coordination of inspection-related activities between competent authorities and audits of inspection systems [4];

(iv) dissemination of the results of its work and the monitoring of uptake of its work.

The rapporteurs of the IES presented the work carried out and outlined next steps, which include the development of the 2019 work. The plan is being finalised.

The ultimate objective is to move to a more operational IES by 2020.

This work of IES is recognised as valuable to increase a common level of knowledge/skills in national authorities. The update on the work of IES will be provided regularly at the CA meetings.

5.2. Other Member State updates on inspections

DG SANTE chair asked CAs if they have any national developments in relation to inspection that they would like to inform the other CAs about. No update was given.

5.3. Update on the GAPP work packages 5 and 6 (blood part) on preparation process authorisation

The EU funded Joint Action, facilitatinG the Authorization of Preparation Process 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, tissues and cells establishments. The action has over 26 associated partners from 17 countries and 14 collaborating organisations. It started in May 2018 and runs for 3 years.

The Blood CAs were given an update on GAPP JA WP 5, developing overall guidance on the organisation of preparation process authorisation and 6, on authorizing changes in activity steps, in particular on deliverables and associated tasks, progress to date, proposals and expected timelines. The authorities were asked to complete the recent survey prepared by the project coordinators.

The progress was welcomed on the GAPP Joint Action, which aims to support authorities to assess and authorize BTC processes.

[4] Point iii covers joint inspections and the CESIP work. Overall, IES has been divided into five work clusters: Inspection Guidelines, Coordination of Training Courses, Coordination of Joint Inspections, Oversight of inspection systems, Dissemination and Monitoring.

6. VIGILANCE AND SURVEILLANCE

6.1. ECDC update

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

These included the detection of Ebola virus disease (outbreak DRC update), Zika virus (ECDC RRA), West Nile virus and USUTU viruses and the consequent challenges for blood safety in the EU.

ECDC also reported on their SoHO activities in 2019. ECDC described the work they have contracted on "Assessing the risk of bacterial infections transmission through SoHO", a new contract on "Assessing the risk and prevention of fungal and parasitic infections transmission through SoHO", an ECDC risk assessment on TBE transmission through SoHO, an update of recommendations on Ebola virus disease and SoHO safety and an expert meeting on pathogen inactivation of blood and blood components.

6.2. Rapid alerts - General overview

DG SANTE provided the participants with a summary of alerts posted in the RAB and RATC platforms up to June 2019.

A number of alerts (epidemiological alerts, Quality and Safety defects, information notices, bilateral enquiries and illegal/fraudulent cases) had been reported via the platform. In total, 25 rapid alerts for blood (RAB) were reported for 2018. In January-May 2019, there were 2 alerts uploaded for blood by the CAs.

Although the number of rapid alerts for RATC reported each year were generally decreasing, 2018 showed an increase.

DG SANTE also noted that a link between RATC and the EU Coding Platform for Tissues and Cells is ready to be tested.

The Commission informed the meeting that activities were summarised in one single 2018 report that was published in March 2019[5].

6.3. Member State surveillance updates

No Member State had specific national surveillance information to report.

6.4. SARE reporting

SARE 2018 exercise (2017 data)

The Council of Europe (EDQM) debriefed the participants on the analysis of the 2018 SARE reporting exercise for Blood. The numbers and types of SAR and SAE reported were presented, along with denominators and the EDQM team highlighted areas where improvements could be made.

[5] https://ec.europa.eu/health/sites/health/files/blood_tissues_organs/docs/2018_ra_soho_summary_en.pdf.

A total of 3114 serious adverse reactions (SAR) (imputability level 1-3) and 1871 SAR (imputability level 2-3) were reported. The most frequently reported SAR were anaphylaxis/hypersensitivity and febrile non-haemolytic transfusion reactions. A total of 2920 serious adverse events (SAE) were reported by the MS with great variability in the numbers reported. Twenty-three Member States reported 4635 SAR in donors on a voluntary basis. In total, 25 million units were issued for transfusion and 20,6 million units were reported as transfused in 2017.

EDQM noted that some countries still do not report any SAE or SAR and do not report all denominators. EDQM proposed steps to improve the exercise, including improving definitions and guidance and mandatory reporting of donor SAR with criteria and definitions.

EDQM noted that the new donor reaction categories introduced by VES helped to clarify which SAR in donors should be reported. As a result MS provided more comprehensible data on SAR in donors. EDQM will provide further information at the next meeting on training for vigilance officers submitting the SARE country reports to the Commission. The training will be carried out by EDQM in the framework of their grant agreement with the Commission.

The Commission thanked EDQM for the efficient way they have carried out this work.

Launch of 2019 exercise (2018 data)

The Commission reminded all participants that the new SARE reporting exercise had been launched in April 2019 with a deadline for submission of 19 July 2019. The Commission highlighted the need for Member States to submit their country reports on time.

The MS were invited to carefully consider the SARE Common Approach document and pay special attention to the changes in the reporting template. If there are two or more CAs in a MS, the representatives were asked to coordinate and send a single submission.

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

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.

The VES had compiled a list of issues that might be addressed to improve the quality and usefulness of the SARE exercise. The VES proposed improvements for 2018-2019, which will be elaborated by three vigilance experts working groups focusing on (i) TC SARE definitions and categories, (ii) BTC SAR and (iii) BTC SAE.

A new wave of proposals for improvement will be discussed and prioritised for possible implementation in the 2019 exercise or beyond. It was reported that the VES will also start to address vigilance issues for organs. It was noted that the next steps will include incorporating proposals in the structure of a web reporting form and drafts to be presented in VES meeting planned in November 2019 and circulated to the NCAs. The VES rapporteur noted that the VES would like to send a questionnaire to the Competent Authorities about the current practices of collecting data for the EU.

DG SANTE supported this initiative and thanked the VES for their work and noted that this expert sub-group is providing an excellent bridge to the vigilance officers in Member States that are completing the SARE submissions each year. The level of activity in the group was clearly high and the results were likely to bring significant improvements.

6.6. Delegation of national vigilance activities by CAs to professional bodies

DK, NL and UK presented plans or positive experiences with delegating vigilance data collection to professional associations.

The UK representative elaborated how MHRA works with SHOT. SHOT (Serious Hazards of Transfusion) is the UK's independent, professionally led, confidential reporting system for serious hazards of transfusion. It is hosted by the UK's NHS Blood and Transplant (NHSBT). MHRA, as the UK's CA, is in charge of reporting SARE to the EU Commission. Collaboration between MHRA and SHOT ensures that there is no duplication of reporting. This allows both MHRA and SHOT to make better informed recommendations on strategies to improve patient safety.

The DK CA considers delegating some of the vigilance work to a professional association. This would enable them to create a common national framework for collating relevant vigilance data by five regions, ensure consistent use of definitions, terminology and the reporting criteria, use professional expertise to evaluate data in a consistent manner and improve compliance with the expectations and regulatory standards etc. The NL representative explained the link and the division of the responsibilities between the NL CA and TRIP.

The SANTE representatives noted, while it is a Member State responsibility to ensure that the legal obligations for vigilance are effectively implemented, the Member States can organise the set-up of national systems in different ways.

7. THERAPY SPECIFIC TOPICS

7.1. Feedback from the T&C competent authority survey and discussion

In the context of the BTC evaluation, DG SANTE had circulated a short survey to the authorities in early 2019 to gather data on three topics, where evaluation data was incomplete. The topics included the classification of certain blood, tissues and cells at Member State level.

The results of the survey on **classification of therapies were presented.** On the classification of a range of specific substances/products, the survey indicated that in some cases Member States apply divergent regulatory frameworks for identical therapies, or, in some cases, no regulation. Specifically, Faecal microbiota transplants (FMT), human breast milk, platelet-rich plasma prepared in the hospital, autologous adipose tissues prepared in the hospital, cells separated by enzymatic digestion without expansion (e.g. keratinocytes and hepatocytes), serum eye drops, demineralised bone combined with gel or putty, decellularised dermis and decellularised heart valves are being regulated in divergent ways across the MS.

In the general discussion, a CA representative drew attention to a written comment submitted with the inputs to the survey: blood cells are excluded from the Medicinal Products Directive (2001/83/EC), and blood and blood components from Tissue and Cells Directive (2004/23/EC). Therefore any product obtained from blood and not intended for transfusion or PMDP but for

any other clinical purpose (e.g. similar to non-homologous use), except of HPSC and DLI, is not regulated on EU level and quality, safety & efficacy is not being assessed on an equivalent level, i.e. monocyte concentrate obtained by apheresis such as EudraCT No: 2012-002814-38), PRP, PRF etc. In the view of that participant, this can pose risks to recipients' health.

Overall, the participants reiterated a need highlighted by the NCA tissue and cells group for more NCA involvement in classification matters, also at EU level. This would address a common concern for more regulatory clarity.

7.2. PRP/PRF – comments from Denmark

The DK delegate gave a short presentation on Platelet Rich Plasma (PRP) and Platelet Rich Fibrin (PRF) and its regulatory status in the EU. The delegate noted that PRP and PRF may fall within different legal frameworks, i.e. medicinal products, blood, tissues & cells.[6]

He noted that as regards the classification of PRP and PRF at the national level, 3 MS regulated these products under the EU tissues and cells legislation, 5 MS - under the EU blood legislation, 2 MS – under the EU medicinal products legislation, 6 MS – no regulation and 3 MS apply other regulatory frameworks.

The delegate noted that there seems to be a general consensus that the subject should be addressed further.

7.3. General discussion on the scope of 2002/98/EC and any regulatory gaps

Some representatives mentioned that the criteria and mechanism for classification of a range of specific blood substances and products are not clear. This leads to diversity of classification approach to components. In their opinion, it is necessary to ensure that there is an appropriate regulatory approach, noting that this would facilitate the innovation and would help clarify ambiguities related to classification.

8. COUNCIL OF EUROPE UPDATE – OTHER ACTIVITIES

EDQM presented their work on contributing to ensuring a high level of quality and safety standards in the blood field and harmonising activities among European countries, facilitating uniform standards and practices. A short update was provided on the status of the newly revised GPG and the 20th edition of the guide.

An overview of EDQM activities in the field of blood as part of the newly signed Grant Agreement between the EDQM and the Commission was also given.

The representative also outlined the progress on the B-PTS and B-QM programmes in 2019[7], both are EU/CoE co-financed programmes. It was highlighted that, in general, European blood testing laboratories have improved their performance. However, issues with anti-treponema assays and Irregular antibodies testing were noted. The EDQM will continue performing 6 B-PTS studies per year and is currently reflecting on the possibility to have a study on bacterial testing.

[6] Cf. Also EDQM Guide for Tissues and Cells, 3rd Edition 2017.

[7] With respect to the B-QM programme, it was noted that the most common findings in the auditing schemes were related to change control, qualification, risk management and cold chain. Thus, the importance for the EDQM to complement the activities with educational tools such as training and guidance documents.

The representative informed the competent authorities of an event that will be organised by EDQM in April 2020 to address emerging issues having an impact on Blood establishments and touch upon the Medical Device legislation and changes in the supply market.

Importantly, EDQM brought to the attention of participants an issue concerning the regulatory classification of disinfectant solutions used in blood establishments. Through auditing schemes, it has been observed that disinfectant solutions were differently classified either as Biocide or as Medical devices. It has been recently observed in some countries that authorities have placed disinfectant solution under the medical device framework. As a result, their price increased by a factor of 8, creating additional costs for the establishments.

A follow-up of an audit performed in Greece was presented. Following the audit, the EDQM team was requested to support Greece in reforming the blood system and in this context was invited to participate in the 11th Panhellenic congress. EDQM considered that Greece would be a suitable applicant for SRSS funding to support this reform.

The Commission and the representatives acknowledged EDQM's work in the field.

9. CLINICAL OUTCOME DATA FOR SOHO

This clinical outcome data/real world data for SoHO session included presentations on the insights of the participants on how donor and patient registries had been established and can be used to improve donation and transfusion programmes. Two blood-specific registries were presented - SCANDAT with data on DK and SE blood donors and recipients, and the DE haemophilia register. The presentations demonstrated the value of long-term follow up e.g. to assess risks of disease transmission and cost/benefit of NAT testing technology.

9.1. Feedback from registries meeting of 20 February2019

DG SANTE debriefed the meeting on the SoHO registries meetings held in 2018 and 2019. The objective was to raise awareness of SoHO registries among authorities and explore their possible future role in the work of the authorities.

Triggered by requests for advice regarding the implications of the General Data Protection Regulation (GDPR) for SoHO Registries, the Commission had convened a first meeting of registries to discuss data protection and other topics of shared interest in 2018. This was followed by a second meeting in -2019. The meetings were attended by representatives from different organisations that host and maintain registries of donors and/or patients. The key topics addressed were compliance with the GDPR, ensuring quality of data in SoHO registries, registry governance, registry sustainability and funding and the potential for the secondary use of data from SoHO registries, e.g. for regulatory or research purposes. A discussion that had arisen in the registry meetings was on the most appropriate roles authorities and professional societies in the collection of data in registries. Participants agreed that data should be shared to keep the collection workload as efficient as possible for the clinicians (collect once, use often). The participants had appreciated the opportunity to share experiences with each other and to discuss the GDPR with Commission experts working on that legislation. A GDPR specific Q&A was prepared for the registry meeting and shared with the NCA's.

9.2. Presentation of SCANDAT registry

An expert gave a presentation on the Scandinavian Donations and Transfusions (SCANDAT) database. SCANDAT is a population-based register for monitoring long-term outcome and possible disease concordance among blood donors and recipients.

The SCANDAT database stores data on blood donors and recipients who have been registered at least once in any of the computerized local blood bank databases in Sweden and Denmark since the start of computerized registration in 1966. The records of these individuals, with their entire computerized donation and/or transfusion histories and all donor-component-recipient connections, were linked to nationwide population and health registers to attain an essentially complete follow-up for up to 36 years regarding reproduction, hospital morbidity, cancer, and death.

The expert noted that, even with appropriate donor deferrals and advanced screening tests, the risk of disease transmission through blood transfusion cannot be completely disregarded. Efficient monitoring of possible disease transmission between blood donors and recipients should be an important component of a comprehensive haemovigilance system. It was concluded that it is possible to use existing computerized data, collected in routine health care and in haemovigilance systems, for monitoring the long-term outcome and disease concordance in blood donors and transfusion recipients.

9.3. Presentation of German Haemophilia Registry

Since 2004, the Paul-Ehrlich-Institut (PEI) has assumed an important role in creating a German Haemophilia Registry, the "Deutsches Hämophilieregister" (DHR). It is a joint project of the two patient organisations, a scientific society and the PEI. In February 2007, during the annual conference of scientific society, a collaboration contract for the establishment and operation of the DHR was signed.

The DHR records online data from patients with haemophilia A, haemophilia B, von Willebrand`s disease and other coagulation factor deficiency disorders since 2009. These data include the number of persons with congenital haemostasis disorders, classified by type of disease and severity as well as patients' age, and the use of clotting factor by patient group.

The DHR is a professional, user-friendly database for online input of data. The evaluation of the data, accumulating prospectively, is organised by the DHR Steering Committee. Contacts were made with international colleagues in the framework of the International Society on Thrombosis and Haemostasis (ISTH), in order to achieve as far as possible a harmonised database structure, enabling concerted evaluations with other international and regional registries.

Since the DHR collects personal health data of patients, special importance was attached to the protection of the patients' personal rights, and particularly, data security. Patient's pseudonymised data is enrolled in the DHR based on an informed consent.

9.4. Update on GAPP work packages 8 and 9

A short update was given on GAPP WP 8 and 9. These WPs cover the use of clinical data for preparation process authorisation and developing a model for an EU database of process authorisations.

9.5. GDPR – questions and answers for the SoHO sector

See point 9.1 above

10. CONTINUITY OF SUPPLY AND EMERGENCY PLANNING – stakeholder session

10.1. Feedback from the Plasma Supply Symposium 20 Feb 2019 – EDQM

EDQM presented feedback from a EDQM/SANTE Plasma Supply Symposium, attended by over 200 participants. The symposium led to the development of recommendations addressing all key players in the supply chain (establishments, authorities, companies, the Council of Europe (EDQM) and the Commission) to support achieving an increased plasma supply. . The recommendations focused on donor vigilance, plasma collection support and achieving strategic independence of plasma in Europe, legal framework concerning plasma donor and donation regulation, plasma collection and a sustainable PDMP supply.

10.2. Report on 2019 Kreuth meeting on PDMP indications and use

The EDQM representative recalled the background of the Kreuth initiative and summarised the results of the 2019 Kreuth symposium,

The Kreuth initiative began in 1999 with an initial symposium founded by the Commission and co-sponsored by the Council of Europe/EDQM, the Ludwig-Maximilian University of Munich (LMU) and the Paul Ehrlich Institute (PEI). This initiative has given birth to a number of non-binding legal instruments, namely Council of Europe Resolutions[8].

The 2019 Kreuth Symposium focused on Optimal Treatment of Haemophilia and aimed at developing recommendations. Following CD-P-TS approval, they will be incorporated in the technical Annex of Resolution *CM/Res(2017)43 on principles concerning haemophilia therapies - replacing CM/Res (2015) 3*.

10.3. Developing guidance on continuity of the blood supply – EDQM

The EDQM representative provided information on the rationale for having a coordinated initiative at European level on emergency and contingency planning. This initiative had been included in the newly signed grant agreement between the European Commission and the EDQM. An expert group will be established for that purpose. A call for nomination of candidates was to be launched by end of 2019.

10.4. Impact of DEHP ban on supply of blood bags

The European Blood Alliance and MedPharmPlast had both highlighted in their responses to the Open Public Consultation for the BTC Evaluation their concerns regarding the inclusion of

[8] Kreuth III: Resolution CM/Res(2015)2 on principles concerning human normal immunoglobulin therapies for immunodeficiency and other diseases. Resolution CM/Res(2015)3 on principles concerning haemophilia therapies
Kreuth IV: CM/Res(2017)43 on principles concerning haemophilia therapies - replacing CM/Res (2015) 3

DEHP on the REACH list and the ban on its use in medical devices. As planned, the Commission had invited these stakeholders to address this topic in this meeting with authorities.

The concerns were expressed in the context of a potential impact of the DEHP ban on the supply of blood bags.

In the meeting, DG GROW outlined the legislative developments from the REACH perspective.

EBA[9] and MedPharmPlast[10] raised the concerns of the blood services and blood bag manufacturers, respectively. Industry signalled that a call to phase out the use of DEHP before 2012, without a validated alternative, brings a high risk of interruption to the supply of blood bags, which are critical for the blood supply. They pointed out that the use of current alternatives would significantly shorten the shelf life of red blood cells. EBA reiterated this message, noting that switching to alternatives without extensive preparation may threaten the blood supply (shelf life, risk of reduced clinical effectiveness) and added that incomplete validation of DEPH free blood bags may lead to life threatening complications. They concluded that an orderly validation of the whole transition to DEPH-free blood collecting systems is needed to guarantee the sufficiency and safety of blood transfusion and transplantation.

Following a public consultation, the SCHEER committee approved guidelines on the benefit-risk assessment of the presence of phthalates in certain medical devices at its plenary meeting on June 18. The Commission noted that the guidelines will be published during the summer of 2019.

Further discussion between all participants was called for on this file with complex interactions involving REACH, medical devices, the SCHEER committee and SANTE/B4. It will be important to follow the developments in this file, given the possible impact on the blood supply.

11. RESEARCH AND DEVELOPMENT – stakeholder session

Stakeholders, including professional associations and industry (EBA, IPFA, EPA, PPTA and EBA) had been invited to present their views on research needs for this sector for the future. A plan to build a strategic SoHO research agenda with RTD was suggested. The meeting was also joined by a representative of DG RTD (Research and Development).

11.1. RTD presentation on Horizon Europe

DG RTD (Research and Development) presented Horizon Europe and the possibilities for funding research in the area of SoHO. An exchange followed with the professional associations on the research needs for the future. The RTD representative asked the authorities to participate in deciding what research topics they would suggest for the future to move the field forward.

11.2. Stakeholder presentations on research priorities

The European Blood Alliance (EBA), the Plasma Protein Therapeutics Association (PPTA) and the European Plasma Alliance (EPA) gave short presentations to highlight the key areas of research

[9] The European Blood Alliance (EBA) is an association of not-for-profit Blood Establishments, with 26 members throughout the European Union and EFTA States. EBA strives towards this mission by assisting our members to improve performance through collaboration, to engage in regulatory affairs to promote best practice and to facilitate information collection and knowledge exchange.

[10] MedPharmPlastEurope (MPPE) is a sector group of the European Plastics Converters representing companies involved in the complete value chain of plastic medical devices in Europe.

that they consider important to improve the safety, quality and sufficiency of the blood and PDMP supply for EU patients in the future, from their perspectives.

The EBA suggested focussing on donors and donation as well as on the transfusion fields. To improve donor health care, they called for long-term follow up of blood donors, big data (registry/ies), multivariate analysis and health-promoting effects should be considered. To promote transfusion safety and efficacy, there is a need to monitor infectious disease transmissions, promote patient blood management and evidence based use of plasma-derived products (PDMPs).

PPTA suggested that the key areas of research should include new clinical indications, the development of new protein and alternative therapies for current indications, novel processes and technological improvements.

EPA noted that the research priorities should focus on donor safety (adverse events, safety of donation process and donor health monitoring including safety of plasma donation) as well as on sufficiency of the plasma supply in the EU and how to broaden the donor base.

11.3 EBA presentation on PBM conference results

EBA gave a presentation on the international consensus conference on Patient Blood Management[11] of 24-25 April 2018 Frankfurt, Germany.

The 2-day International Consensus Conference gathered 200 medical experts from 5 continents representing more than 10 disciplines (e.g. transfusion medicine, surgery, anaesthesiology and haematology)[12].

The main objective of the PBM conference was to formulate evidence-based recommendations. The conference defined the current status of the PBM evidence base for practice and research purposes and established 10 clinical recommendations and 12 research recommendations for preoperative anaemia, red blood cell (RBC) transfusion thresholds for adults and implementation of PBM programs. In particular, for preoperative anaemia, the recommendations included detection and management of anaemia sufficiently in advance of major elective surgery. For RBC transfusion thresholds, the recommendations considered critically ill, but clinically stable, intensive care patients with or without septic shock as well as patients undergoing cardiac surgery. For implementation of PBM programs, the recommendations were developed to implement comprehensive PBM programs and to use electronic decision support systems to improve appropriate RBC utilization.

12. PRESENTATION OF OTHER EU-FUNDED ACTIVITIES

12.1 Other GAPP work packages

FI presented GAPP WP 7 that is developing a technical annex to the overall guidance, assessing the quality and safety of donor testing, pathogen reduction and sterilization steps as part of preparation process authorisation. For this WP, five sub-groups had been established. Existing guidelines will be taken into account, including the guidelines produced by EDQM (e.g. guide to the preparation, use and quality assurance of blood components, Guide to the quality and

[11] Patient blood management (PBM) is a patient focused, evidence-based and systematic approach to optimize the management of patients and transfusion of blood products for quality and effective patient care.
[12] https://research.monash.edu/en/publications/patient-blood-management-recommendations-from-the-2018-frankfurt-.

safety of tissues and cells for human application and the European Pharmacopoeia), EAM (Quality and Safety Guidelines), ICH (Quality and Safety Guidelines), ESHRE (Guidelines – good practices) and national guidelines. Progress had been made and the detailed plan of the deliverable submitted.

12.2. Transpose project

The Transpose representative could not attend the meeting on this occasion. The participants were reminded that slides with an update of the project had been shared in CircaBC.

13. EMA UPDATE

The EMA representative could not attend the meeting on this occasion.

14. WHO UPDATE

WHO presented the draft WHO Action Framework to Advance Universal Access to Quality and Safe Blood and Blood Components for Transfusion and Plasma Derived Medicinal Products. The draft document provides strategic direction to the work of WHO by addressing the present barriers to availability, quality and safe blood and blood products and by building up on existing and future WHO partnerships in the field.

NCAs will be consulted on further drafts when available.

15. ANY OTHER BUSINESS

DG SANTE will organise a conference on the results of the BTC evaluation on 28 October 2019 in Brussels. The participants were asked to save the date.

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 competent authorities is planned for the first half of 2020 (now confirmed for the 18-19 February 2020).