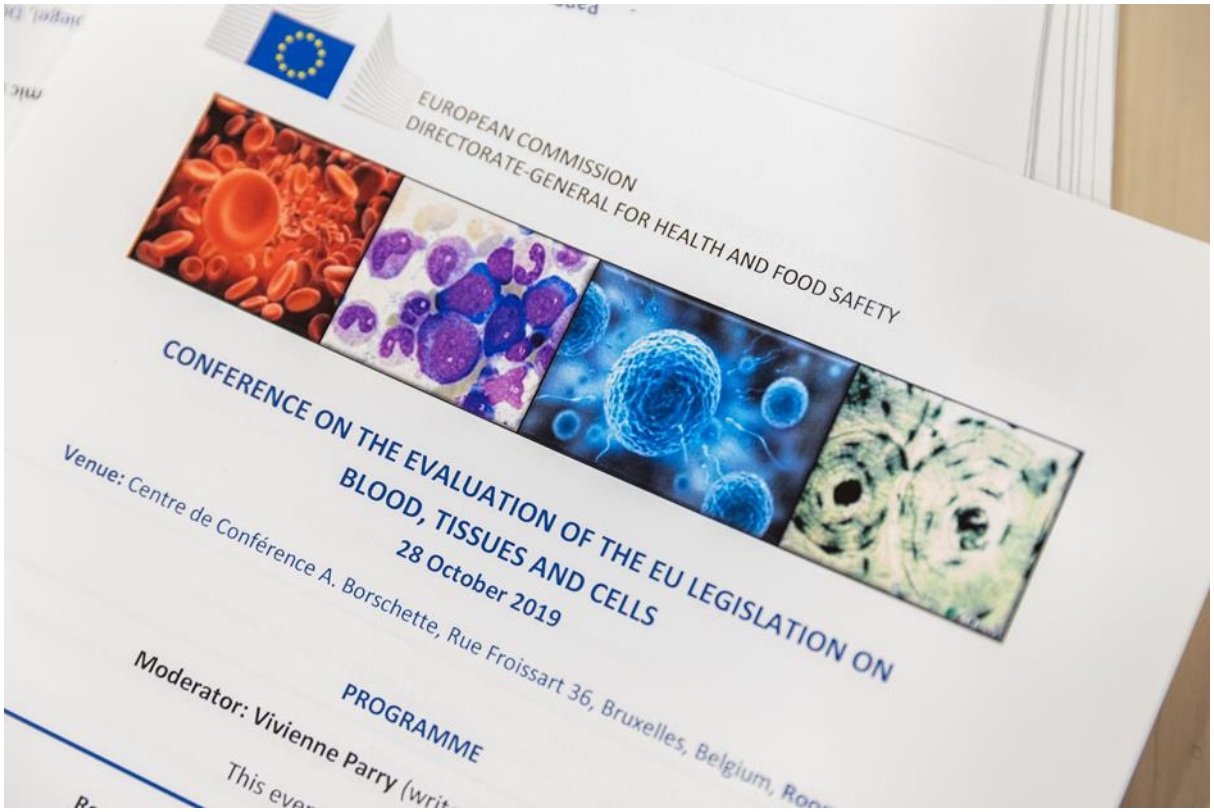
EUROPEAN COMMISSION
DIRECTORATE GENERAL FOR HEALTH AND FOOD SAFETY

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

Brussels, 2020
SANTE B4

Summary of the Conference on the Evaluation of the EU Legislation on Blood, Tissues and Cells

Brussels, 28 October 2019



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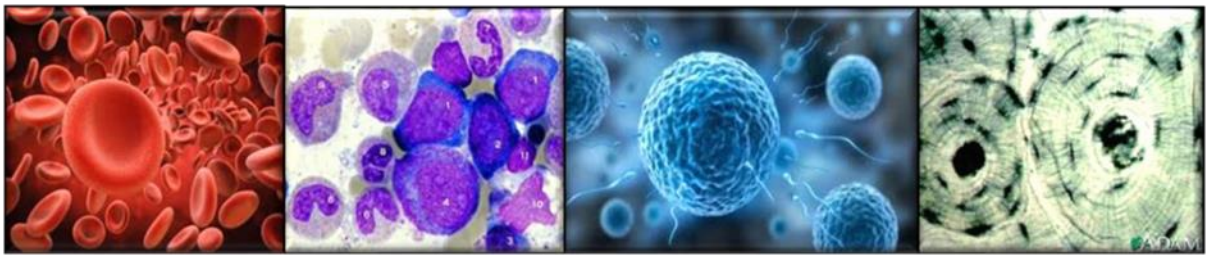
This report summarises discussions at a Stakeholder Conference organised by DG Health and Food Safety in the context of an Evaluation of the EU Legislation on Blood, Tissues and Cells. It provides background information about the event and summarises the key issues raised by stakeholders.

Further information, including recordings of the event, can be accessed here:

https://ec.europa.eu/health/blood_tissues_organs/events/ev_20191028_en



BACKGROUND

The Evaluation of the Blood, Tissues and Cells Legislation

On 11 October 2019, the Commission published its Evaluation on the EU legislation on blood, tissues and cells (BTC). This was the first evaluation of the legislation since the adoption of the basic Acts in 2002 (blood) and 2004 (tissues and cells). The aim of the legislation was to harmonise heterogeneous Member State practices through common and binding standards for quality and safety, ensuring the availability and exchange of safe blood, tissues and cells and enhancing donor and recipient confidence in the processes of donation, transfusion, transplantation and assisted reproduction.

Since then, these Directives have both been complemented by several implementing Commission Directives specifying more technical requirements. The Directives place obligations on several sub-groups of professionals working with blood, tissues and cells, in particular in the following areas:

- Blood and blood components for transfusion
- Plasma for manufacturing of plasma-derived pharmaceuticals
- Gametes and reproductive tissues for assisted reproduction
- Haematopoietic stem cells from bone marrow, peripheral blood or cord blood for transplantation
- Replacement tissues such as skin, bone, cornea or heart valves for transplantation.

The evaluation was conducted in line with the Commission's Better Regulation Guidelines and aimed to assess whether the legislation achieved its original objectives and whether it is still fit for purpose. The evaluation consisted of several steps, starting with the publication of a Roadmap in January 2017 and including a study by an external contractor and extensive consultation of stakeholders.

Stakeholder Consultation included an Online Public Consultation launched on May 29th, 2017 and running until September 14th. Submissions were received from 158 organisations and 43 citizens. Meetings with key stakeholders were held throughout the period of the evaluation to gather focused and specific input through direct interaction. A Stakeholder Event on September 20th, 2017 was attended by over 200 stakeholders. The Evaluation Roadmap, External Study, Summary minutes of meetings with stakeholders, Summary of the Stakeholder Event and the final Evaluation itself are published on a dedicated DG Santé webpage[1].

The Stakeholder Conference

Following the publication of the BTC Evaluation, the Commission organised this conference to present the findings and give stakeholders an opportunity to discuss them. The conference was open to all interested organisations and individuals.

The Conference Programme was structured around a series of themes emerging from the evaluation. For each session, the Commission summarised the findings on a specific topic

[1] https://ec.europa.eu/health/blood_tissues_organs/policy/evaluation_en

and a panel of stakeholders made short statements, followed by a moderated discussion with participants. The final session included a panel of leaders of EU and international institutions that discussed future strategies for the field. The conference programme is presented in Annex 1. The Conference was moderated by Vivienne Parry, a UK broadcaster and journalist. Short curricula of the panellists, the slides they presented and links to recordings of the full conference are available online[2].

The Conference in numbers

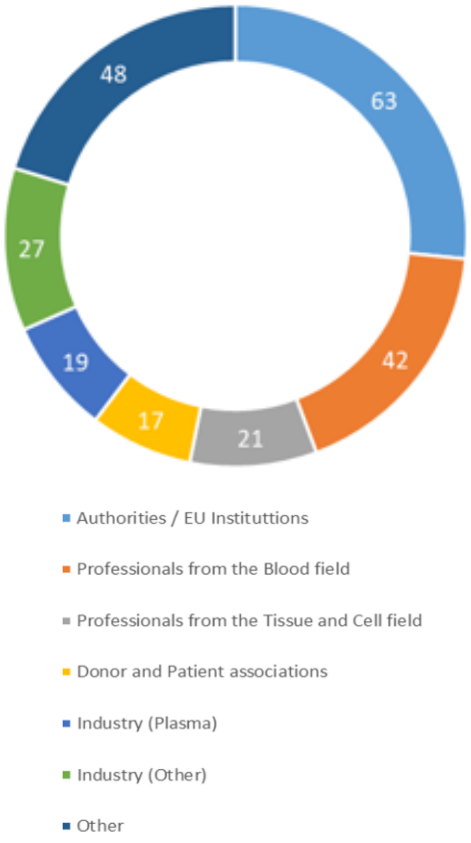


Figure 1: Participants by stakeholder group

The event was attended by 237 participants, from all 28 EU Member States, as well as from the USA, Norway and Switzerland. The audience represented a variety of sectors and stakeholders, as shown in Figure 1.

[2] https://ec.europa.eu/health/blood_tissues_organs/events/ev_20191028_en

OPENING REMARKS

The conference was opened by Anne Bucher, Director General for DG Health and Food Safety (DG SANTE). She welcomed the large number of stakeholders representing a wide range of interests and thanked the participants for their active participation in the evaluation process. She noted the critical importance of the field for the millions of patients across the European Union (EU) that are treated with donated blood, tissues and cells every year.

The Director General noted that the Evaluation had highlighted the overall positive impact of the legislation, adopted in the wake of wide-scale infectious disease transmission by transfusion and transplantation across the EU. She also acknowledged, however, that it had identified important shortcomings that would need to be addressed to ensure a future-proof framework for this sector going forward.

AN OVERVIEW OF THE BTC EVALUATION PROCESS AND KEY FINDINGS

Anna-Eva Ampelas, Head of Unit SANTE/B4: Medical Products - Quality, Safety and Innovation, summarised the process that was followed in the 2-year period leading to the publication of the BTC Evaluation on 11 October 2019 and summarised the key findings around which the programme for the conference was structured.

RESULTS, STATEMENTS AND DISCUSSIONS

Panel 1: The challenge of keeping legislation up-to-date in a dynamic sector with changing risks.

The Commission summarised the main findings of the evaluation for this topic. The key message was that there has been significant technological, epidemiological and societal change in the field, coupled with increased innovation in recent years. The current legislation is very detailed and it is challenging to update it frequently and in a timely manner. However, expert guidance is available that is frequently updated by bodies such as the European Centre for Disease Prevention and Control (ECDC) and the European Directorate for the Quality of Medicines (EDQM, Council of Europe). Gaps have emerged for substances of human origin that do not meet the scope and definitions of the BTC legislation but that could be appropriately regulated under the Treaty mandate – e.g. faecal microbiota transplants, human breast milk, autologous serum eye drops.

This summary was followed by statements from key stakeholder organisations (see Annex 1) and an open discussion with participants. The following key points were raised by the stakeholders:

- There have been significant technological, epidemiological and societal changes coupled with increased innovation in this sector in recent years. – The legislation needs to address these changes in the future.

- Some provisions of the current legislation are too detailed and include outdated technical requirements. This problem needs to be addressed in a flexible manner given the challenges associated with updating the legislation frequently and quickly.

- There is a need to make better use of and establish a stronger role/closer cooperation with expert bodies such as ECDC and EDQM (Council of Europe) taking into consideration the risk- and evidence-based approach undertaken by these organisations. Such expert bodies should work in a fully inclusive and transparent manner.

- There are gaps in the scope of the legislation, which have led to divergent regulation of new SOHO (e.g. faecal microbiota transplants, breast milk, autologous serum eye drops) in Member States. The quality and safety concerns associated with these are consistent with those already addressed in the BTC sector.

Panel 2: The challenge of ensuring that all EU citizens affected by the BTC chain are protected

The Commission summarised the key findings of the evaluation for this topic, noting that there are limited provisions in the current BTC legislation to protect donors. This applies to the rules for donor eligibility, for vigilance and for long-term follow up. Gaps were also identified in the protection of the offspring born from donated sperm, eggs and embryos, including donor genetic testing rules and the follow-up of children born from Medically Assisted Reproduction.

This summary was followed by statements from key stakeholder organisations (see Annex 1) and an open discussion with participants. The following key points were raised by the stakeholders:

- The limited provisions to protect donors in the current legislation are not adequate and this needs to be addressed. Such measures might include donor registries, short- and long-term follow up of donors, donor education, donor studies, enhanced reporting of donor adverse reactions.

- The protection of donors applies to different kinds of living donors but also to different degrees of risk associated with the complexity and/or frequency of the donation. Risks may be exacerbated by increasing commercialisation, e.g. for plasma and egg donation. This should be taken into account in any proposals for changes to the legislation.
- Any changes to donor safety provisions or to donor selection criteria should be undertaken on the basis of clear scientific evidence and with input from all relevant stakeholders in a transparent way.
- Protecting donors is key to maintaining high levels of quality and safety of donated BTC and public confidence in the system. Some stakeholders considered that there is a link between voluntary unpaid donation (VUD) and quality and safety. Others proposed a focus on increased donor health monitoring, rules on donation frequency/volumes and more research on donor health as representing the way forward.
- There are specific challenges associated with Medically Assisted Reproduction technologies, which need to be addressed, e.g., donor anonymity vs. traceability, protection and follow up of gamete donors, genetic testing of donors, and the protection of children conceived using donor gametes.

Panel 3: The challenge of providing appropriate and robust oversight

The Commission summarised the key findings of the evaluation for this topic. Principles to ensure independence of authorities/inspectorates from the field they regulate are lacking and there is no formal mechanism to verify the effectiveness of inspections and authorisations (as seen in other frameworks). The current fixed 2-yearly inspection frequency is not optimal for efficiency or effectiveness of inspection programmes. Provisions for activity data reporting and vigilance reporting are not adequate to facilitate a clear picture of sufficiency and risk across the EU.

This summary was followed by statements from key stakeholder organisations (see Annex 1) and an open discussion with participants. The following key points were raised by the stakeholders:

- There is a need for the BTC legislation to ensure independence of authorities/inspectorates from the field they regulate, similar to other legislative frameworks.
- There is an EU added value of inter-Member State collaborative work on oversight, notably on inspections and vigilance. Moreover, there is a need for further work aimed at increasing mutual trust, e.g., development of clear definitions and guidance, performance of audits and joint inspections and training of inspectors in order to facilitate cross-border exchange and optimise patient access.
- There is a need to move towards risk-based inspection planning.
- A clear view of demand, supply, numbers of donations, volumes of import etc. could help Member States to accurately assess the frequency of adverse incidents and to plan for achieving European self-sufficiency. This will require clear, purposeful, 'minimum' data reporting requirements.

Panel 4: The challenge of facilitating innovation in BTC for patient benefit.

The Commission summarised the key findings of the evaluation for this topic. The evaluation found that the requirements for authorisation of new BTC processing steps are not adequate, particularly in that they do not include sufficient provisions for proof of effectiveness in patients. The exclusion of BTC that are used during the same surgical procedure, or in some cases

processed with medical devices at the patient's bedside, is no longer adequate in view of the medical developments seen in hospitals. In some cases, there is a lack of clarity at borderlines with other frameworks (particularly medical devices and ATMPs). In addition, some donation and testing requirements for BTC that are used to manufacture medicinal products or medical devices are not considered appropriate.

This summary was followed by statements from key stakeholder organisations (see Annex 1) and an open discussion with participants. The following key points were raised by the stakeholders:

- There has been a high level of innovation in the BTC sector in recent years. Clinical data/studies should support the authorisation of new BTC processes/products in some circumstances. The requirements for such data should be proportionate to the risks/degree of innovation involved.
- BTC innovation occasionally crosses/combines different sectors (BTC/Medicinal Products/Medical Devices). This can create challenges and uncertainty in the classification of products/substances, which can be a disincentive for development.
- There is a need for clarity and predictability for innovators/developers/BTC establishments, early in the development process, on the regulatory requirements that will be applicable, especially for borderline products. In this context, it is important that authorities work together across sectors, preferably at EU level (BTC/Medicinal Products/Medical Devices), fostering international convergence of requirements wherever possible.
- There is a specific need to clarify the safety and quality requirements for BTC that are used as starting materials to manufacture medicinal products or medical devices. A requirement to educate and provide appropriate transparent information to donors on the possible uses of donated tissues and cells in commercial contexts is important.
- In the context of the 'same surgical procedures' and use of bedside/in-surgery medical devices for BTC processing, there are regulatory gaps that should be addressed in BTC legislation.

Panel 5: The challenge of achieving sufficiency and a sustainable supply to meet patient need

The Commission summarised the key findings of the evaluation for this topic. It was found that EU Member States often need to rely on the US for sufficient supply of plasma and of some tissues. Furthermore, some barriers for the exchange of BTC between Member States were detected, which can be problematic in case of a shortage of supply. The evaluation identified a lack of provisions for emergency preparedness in the current legislation.

This summary was followed by statements from key stakeholder organisations (see Annex 1) and an open discussion with participants. The following key points were raised by the stakeholders:

- There is a reliance on the US for sufficient plasma for the manufacture of plasma-derived medicinal products (PDMPs) and for the supply of certain tissues. It was noted that for patients relying on PDMPs, supply has become a main safety issue and there was a call for future EU BTC legislation should be both donor and patient centred. In this context, there is a need for action to increase sustainable and safe BTC collection and a sufficient supply in the EU to ensure patient can access the treatments they need while respecting the principle of VUD and the need to protect donors.

- Actions may include encouragement of donation, increasing the use of plasmapheresis programmes, promoting optimal use of BTC and reporting activity data routinely to authorities. These measures could be complemented by requirements for rapid notification to authorities in the event of sudden shortages and the establishment and implementation of contingency plans for emergencies (e.g. epidemiological outbreaks) with a need to clarify the role every party has to play;
- In the context of plasma for the manufacture of PDMPs, it was noted that a small number of EU member states collect significantly more plasma than the others and that these countries have implemented the model of co-existence of public (VUD) and private (allowing compensation of plasma donors) plasma collection systems. Some stakeholders supported the view that this model should be more widely applied to achieve increased plasma collection in Europe. Others considered that increased collection in those countries that rely on pubic or non-profit plasma collection, without donor compensation, should be the focus of efforts to increase plasma supply and ensure that all Member States make a strong contribution. It was noted that clarification in the legal definitions of VUD and of compensation would be helpful.
- It was acknowledged that BTC supply depends on the availability of the medical devices needed to support it.
- There are challenges in the exchange of BTC across borders (e.g. more stringent requirements applied in some Member States). It is important to ensure that availability of BTC substances for patients and EU added value is optimised.

SUMMARY AND THE WAY FORWARD – A MODERATED DISCUSSION WITH A PANEL OF KEY EUROPEAN AND INTERNATIONAL PARTNERS

The panel

The closing panel included representatives of key international partners: The World Health Organisation (WHO), the European Centre for Disease Prevention and Control (ECDC) and the Council of Europe (European Directorate for the Quality of Medicines, EDQM). A representative of the Croatian Ministry of Health also addressed the audience, in the light of the upcoming Croatian presidency of the European Council.

Key points raised in the panel discussion

The discussion with the high-level panellists was structured by a series of questions posed by the conference moderator. The questions focused on the challenges that had emerged in the evaluation and on the importance of international collaboration in finding appropriate solutions.

The Director **ECDC**, Andrea Ammon, emphasized that microbial safety, which is only a part of blood, cells and tissues supply systems, is also only a fraction of the activities covered by ECDC. Nevertheless, it has paramount importance for both donors and recipients of blood, cells and tissues, and public health. In recent decades, the world including Europe is experiencing an increasing number of outbreaks and spread of emerging and re-emerging infectious diseases (EID). The European Union and European Economic Area (EU/EEA) countries may be, in the future, at risk of EID outbreaks which can endanger the microbial safety of blood, tissues and cells and may cause shortages of these products. Through its activities, ECDC will, therefore, continue

to provide the Commission with scientific evidence and suggest interventions to effectively and efficiently address challenges to the microbial safety of blood, tissues and cells. Collaboration between the Commission and ECDC should also be focused on the early detection and communication of cases, to prevent further spread of infections via substances of human origin (SoHO). On the other hand, cooperation in developing and applying effective and affordable preventive interventions (such as laboratory screening and pathogen reduction technologies) may increase the microbial safety of SoHO and prevent unnecessary deferrals of donors during outbreaks.

The Director of **EDQM**, Susanne Keitel, highlighted that EDQM and the EU are placed in a unique situation to contribute to the safety and quality of BTC products. This will lead to safer and more effective treatment of patients and protection of donors. Ensuring an effective regulatory oversight was stressed as an important element. She agreed that technical standards, such as set out in the EU BTC directives, cannot keep pace with ongoing scientific and medical advances. They can also not provide the level of detail required by BTC establishments to deliver safe and effective products and required by competent authorities as the basis for an effective inspection process. She noted that the European Commission and EDQM have established a very fruitful cooperation and they have an opportunity to further reinforce synergies in the field. She considered that the Blood and Tissue and Cell guides published by EDQM are the most effective tools to breach the gaps between the legislative principles and the reality of changing practice, noting that they are regularly updated and support the implementation of the EU directives in a practical manner. She stressed that, in times of limited resources, and while the Member States are under heavy financial burden, avoiding duplication and fostering the synergies is a must. She concluded, stating that the collaboration between the Commission and EDQM should be further nurtured to contribute to the health of European patients.

François-Xavier Lery, Coordinator for Technologies Standards and Norms at the **WHO** headquarters noted that the same challenges to have harmonized standards in place for BTC in the EU are also present in the other WHO member countries. He suggested that the aim should be for

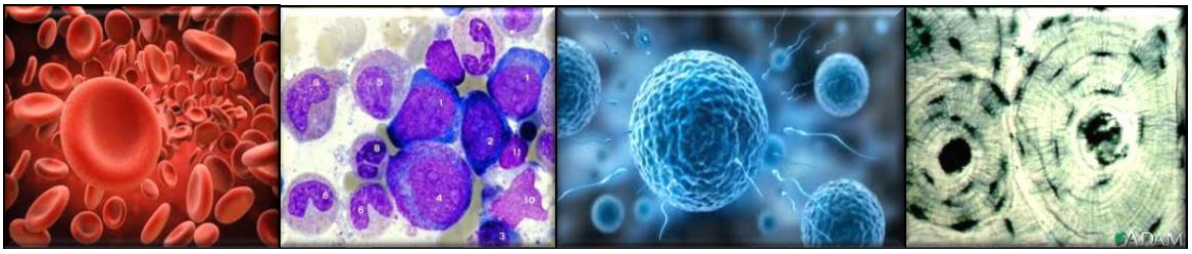
harmonized standards and recommendations across the globe. WHO, as an intergovernmental standard setting organization, has the duty to promote those standards and norms and collaborate with countries and regions to promote their implementation. Working together on a global level is important as BTC are crossing borders. He also reiterated the need to ensure an independent oversight system and highlighted the importance of promoting voluntary and unpaid donation (VUD). He noted that the EU has implemented good practices that should be shared with and implemented in other WHO member countries. The introduction of harmonized terminology and definitions will be important also with respect to donor questionnaires and subsequent evaluation of collected data. The WHO puts effort into explaining the rationale behind the EU approach and its effects to other regions. EDQM guides are being considered beyond the EU, i.e. by the WHO member states. The WHO representative expressed his appreciation that the Commission has taken an approach to widely consult the BTC stakeholders on this evaluation.

The **Croatian** representative, Goranka Marusic Kontent, explained that Croatia will hold the next Council Presidency and that they have put organ donation and transplantation as one of their presidency priorities in health. The Croatian presidency planned to organize a ministerial conference on Organ Donation and Transplantation on 16-17 March 2020 in Zagreb. Considering that Croatia has been particularly successful in building its organ transplantation system, they plan to promote this activity in the EU. Ms Marusic Kontent noted that the evaluation on the EU BTC legislation had provided a good insight into what needs to be done to change the BTC legislation. Croatia understands that there is a need to consider revision of the EU BTC legislation. Areas that require special consideration are donor protection and offspring protection. They hope that some of Croatia's success in the field of organ transplantation could be transferred to the BTC area. Croatia considers that the organizational model and ethical principles of non-commercialization and self-sufficiency in organ donation and transplantation could be mirrored in the tissues and cells area.

CLOSING REMARKS

The Deputy Director General of DG SANTE, Mr Martin Seychell, addressed the conference with closing remarks. He noted the large number of participants, which he saw as a reflection of the importance of the BTC field for EU citizens. Mr. Seychell expressed his gratitude to all the professionals and BTC donors that make essential services for patients, such as blood transfusions and complex cell-based therapies, possible. He also thanked all the stakeholders for their interest and engagement in the evaluation, as well as all the conference panellists for their insightful presentations during the day. Concerning the future, Mr. Seychell emphasized the key need for international organisations and institutions to work together in the BTC field and he stated that the Commission will collaborate closely with its partners on the international level. He explained that the Commission will now move forward to consider the next steps that can be taken based on the results of the evaluation. He confirmed that all stakeholders will be kept informed on this process and stated that continued contributions, suggestions and comments by the stakeholders will be welcomed. Lastly, he highlighted the need to not consider this topic 'in isolation', explaining it will be linked with other priorities on the Commission health agenda, including innovation and access to treatment, the use of data to support policy making and the need to have competitive and innovative treatments available for EU patients.

ANNEX 1: Conference Programme



CONFERENCE ON THE EVALUATION OF THE EU LEGISLATION ON BLOOD, TISSUES AND CELLS

28 October 2019

Venue: Centre de Conférence A. Borschette, Rue Froissart 36, Bruxelles, Belgium, **Room 0A**

PROGRAMME

Moderator: Vivienne Parry (writer and broadcaster)

9.00 – 10.00	**Registration and Coffee**
10.00 – 10.10	**Welcome** **Anne Bucher, Director General, DG SANTE**
10.10 – 10.30	**An Overview of the BTC Evaluation Process and key findings** **Anna Eva Ampelas, Head of Unit B4, DG SANTE**

10.30 – 11.30	**Panel 1: The challenge of keeping legislation up-to-date in a dynamic sector with changing risks**
	- **Presentation of evaluation findings** – Stefaan van der Spiegel, DG SANTE
	- **Panellist reactions:**
	  ○ European Blood Alliance - Philippe Vandekerckhove
	  ○ European Association for Tissue and Cell Banks - Jacinto Sanchez
	  ○ European Society for Blood and Marrow Transplant - Jurgen Kuball
	  ○ European Eye Bank Association - Diego Ponzin
	  ○ European Centre for Disease Prevention and Control - Dragoslav Domanovic
	- **Moderated discussion with participants**

11.30 – 12.30 **Panel 2: The challenge of ensuring that all EU citizens affected by the BTC chain are protected**

- **Presentation of evaluation findings** – Ingrida Pucinskaite, DG SANTE
- **Panellist reactions:**
  - International Federation of Blood Donors - Alice Simonetti
  - European Society for Human Reproduction and Embryology - Kersti Lundin
  - European Plasma Alliance - Matthias Gessner
  - World Marrow Donors Association - Lydia Foeken
- **Moderated discussion with participants**

12.30 – 13.30 **LIGHT LUNCH** – outside the room

13.30 – 14.15 **Panel 3: The challenge of providing appropriate and robust oversight**

- **Presentation of evaluation findings** – Richard McGeehan, DG SANTE
- **Panellist reactions:**
  - BTC Inspectors Expert Sub-group - Lea Joos
  - SoHO Vigilance Expert Sub-group - Jo Wiersum
  - EDQM Tissue and Cell Data Reporting Group - Marta Lopez Fraga
  - Consortium of Representative SoHO Societies - Eoin McGrath
  - DG SANTE, Directorate on Health and Food Audits and Analysis - Daniel Menendez
- **Moderated discussion with participants**

14.15 – 15.15 **Panel 4: The challenge of facilitating innovation in BTC for patient benefit**

- **Presentation of evaluation findings** – Deirdre Fehily, DG SANTE
- **Panellist reactions:**
  - The GAPP Joint Action (BTC Authorities) – Giancarlo Liumbruno
  - International Society for Cell Therapy - Owen Bain
  - Alliance for Regenerative Medicine - Annie Hubert
  - Consortium of Representative SoHO Societies - Esteve Trias
- **Moderated discussion with participants**

15.15 – 15.30	**COFFEE – outside the room**

15:30 – 16:30	**Panel 5: The challenge of achieving sufficiency and a sustainable supply to meet patient need** - **Presentation of evaluation findings** – Stefaan van der Spiegel, DG SANTE - **Panellist reactions:** ▪ Patients relying on plasma derived medicinal products (IPOPI/PLUS) - Johan Prevot ▪ Plasma Protein Therapeutics Association - Jan Bult ▪ International Plasma Fractionators Association - Paul Strengers ▪ Medtech Europe - Nigel Talboys ▪ EDQM - Marie Laure Hecquet - **Open discussion with participants**
16.30 – 17.30	**Summary and the Way Forward** - **Summary of the evaluation findings and the key points raised at the Conference -** Anna Eva Ampelas, Head of Unit B4, DG SANTE - **Collaboration moving forward – a moderated discussion with a panel of key European and International BTC partners** ▪ **WHO - François-Xavier Lery, Coordinator for Technologies Standards and Norms** ▪ **ECDC - Andrea Ammon, Director** ▪ **Council of Europe (EDQM) - Susanne Keitel, Director** ▪ **Ministry of Health, Croatia - Branka Golubić Ćeplic** - **Open discussion with participants** **Closing remarks** **Martin Seychell, Deputy Director General, DG SANTE**

17.30 – 18.30	**NETWORKING RECEPTION**